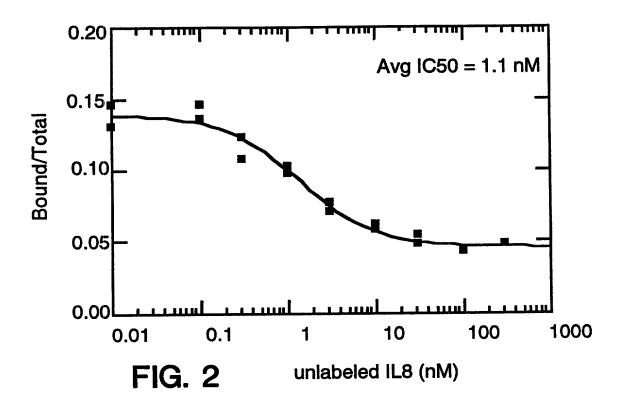
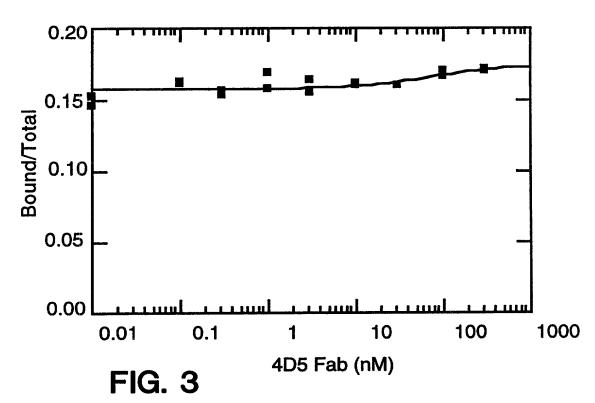
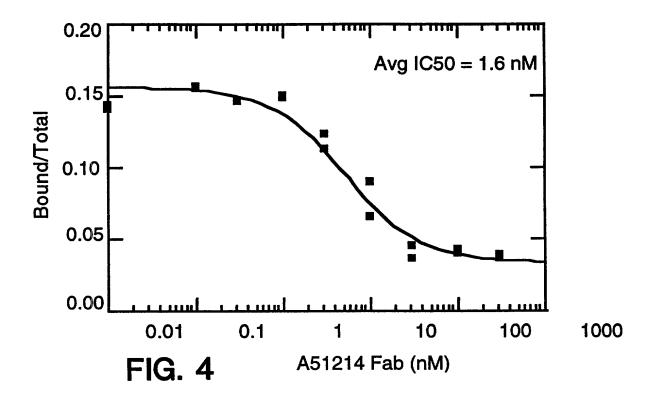
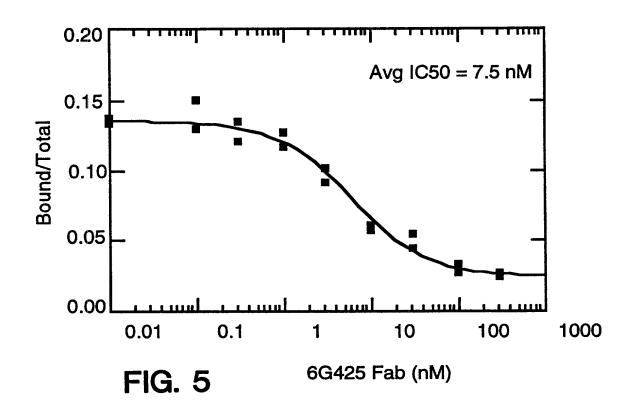
O IL-8 (50 nM)/5.12.14
O IL-8 (500 nM)/5.12.14
D IL-8 (50 nM)/gp 120
O IL-8 (500 nM)/gp120 mAb 5.12.14 conc. (nM) 1000 표 교 1.5-2.5 21 0.5-က် Absorbance (405 nm)









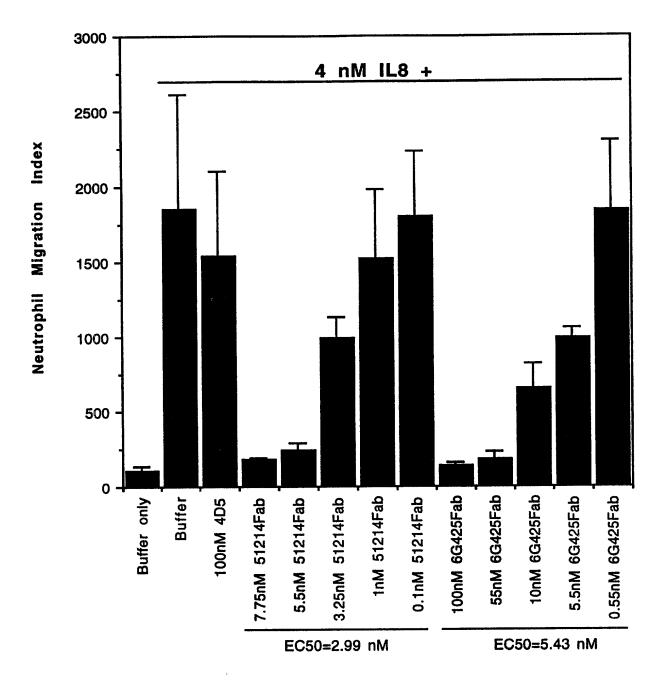


FIG. 6

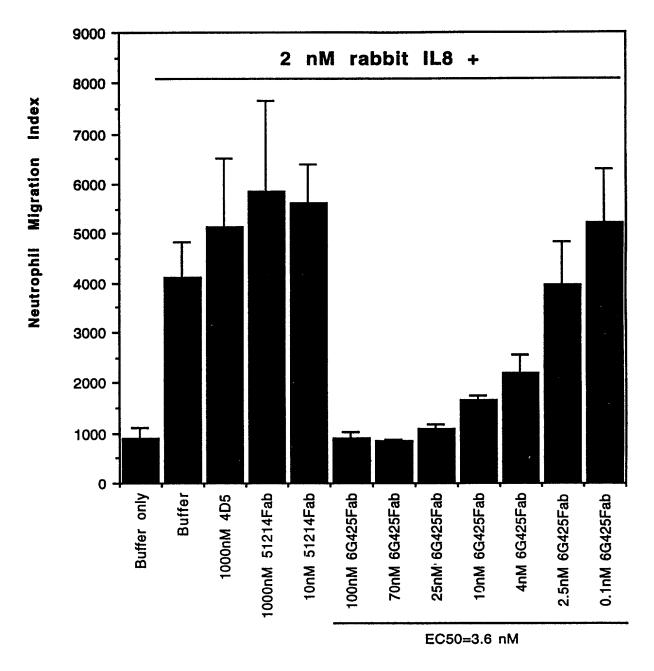
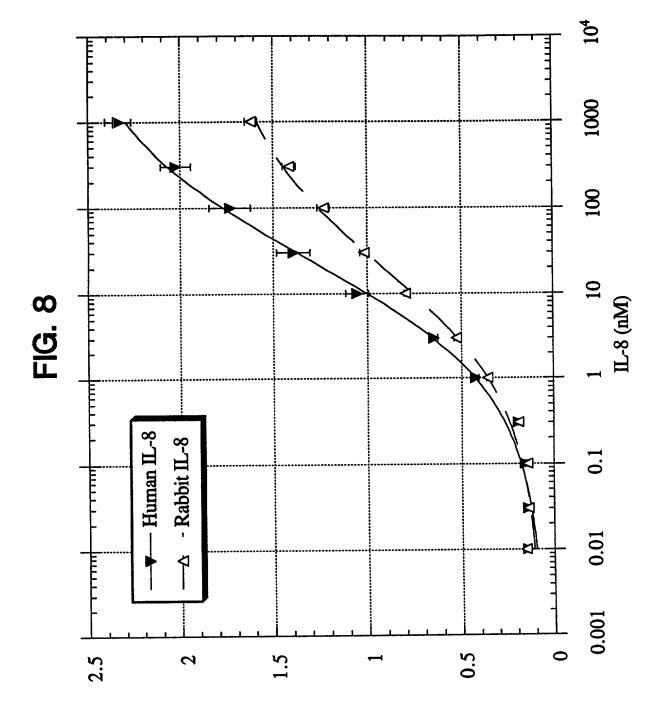


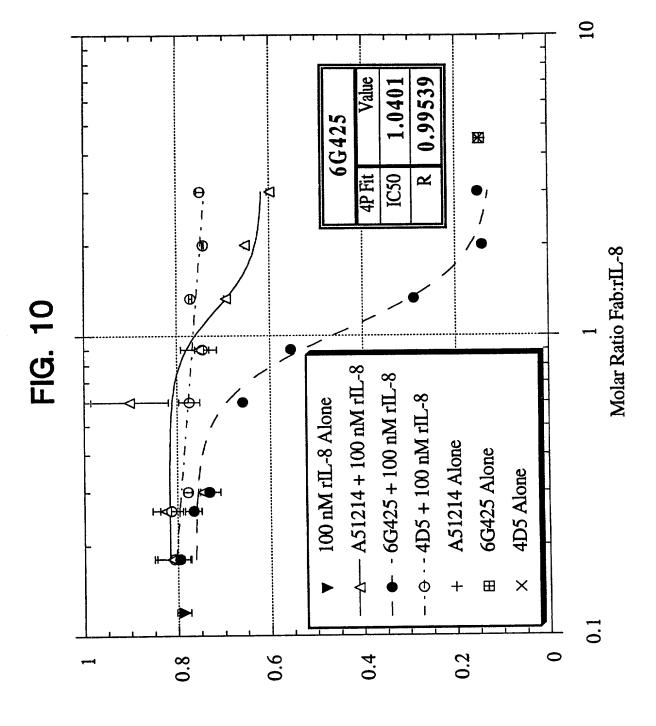
FIG. 7

Absorbance (405 nm)

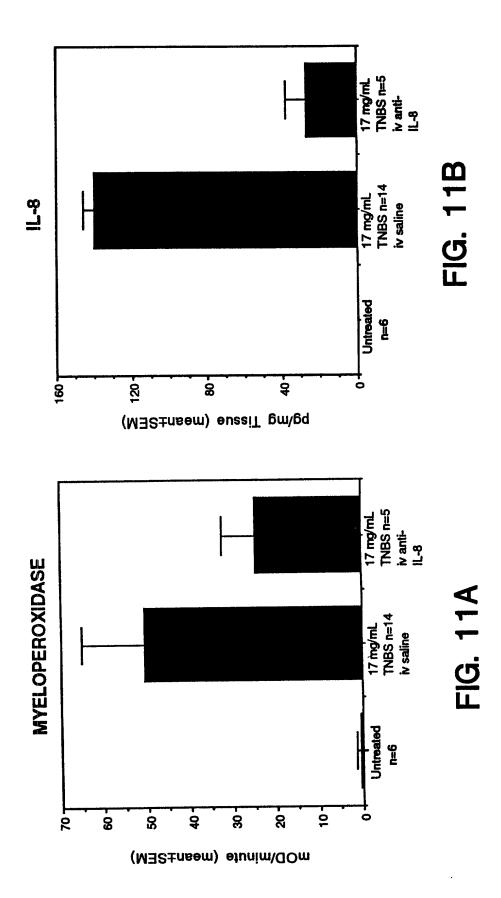


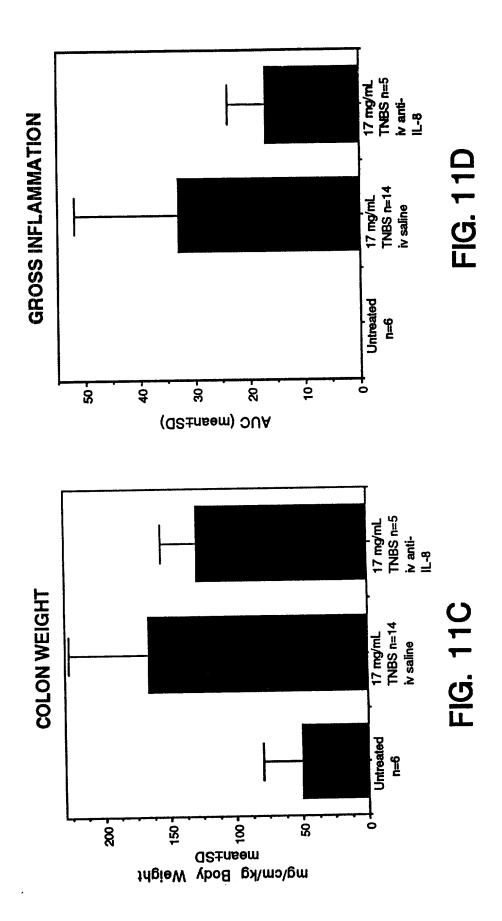
- A51214 + 100 nM IL-8 - 6G425 + 100 nM IL-8 10 100 nM IL-8 Alone - . 0 · - 4D5 + 100 nM IL-8 A51214 Alone 6G425 Alone 4D5 Alone ⊞ X Molar Ratio Fab:IL-8 FIG. 9 Value 0.99536 0.64280.63510.99813 6G425 C30 20 4 120 80 9 0 100

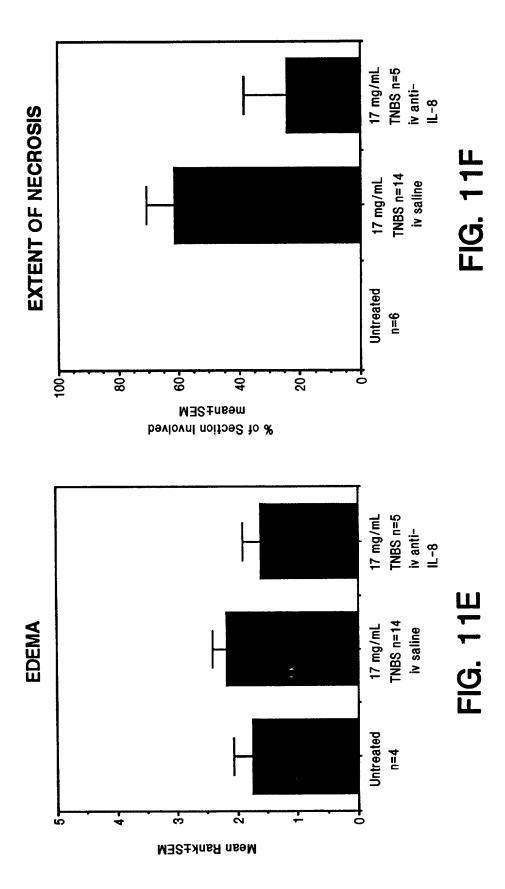
% IL-8-Stimulated Elastase Release

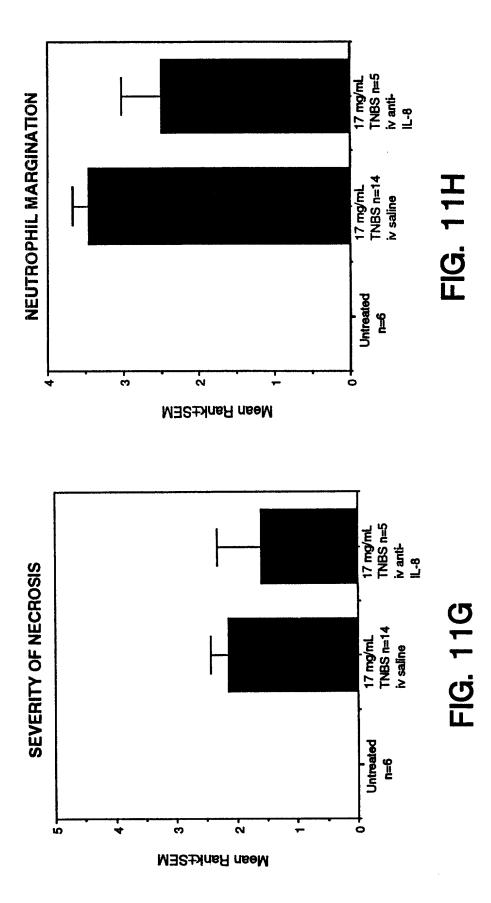


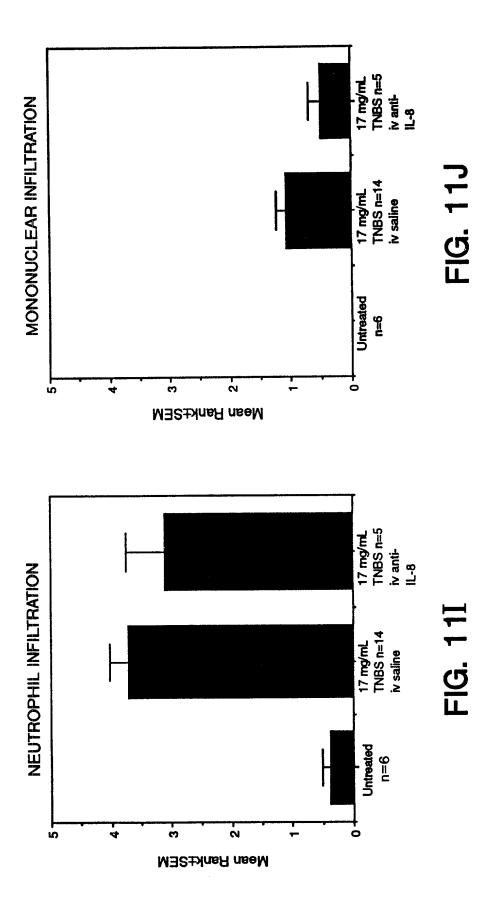
Absorbance (405 nm)

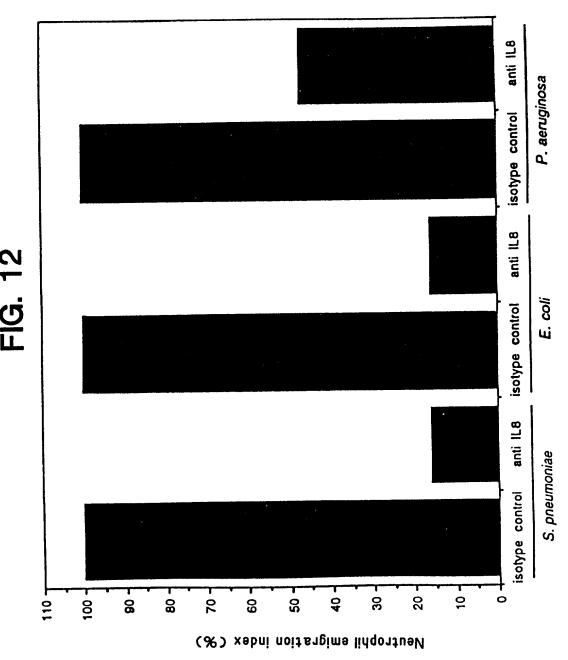












Group (n=5 rabbits per group)

Light Ch	nain Primers:	
MKLC-1,	22mer FIG. 13	
5'	CAGTCCAACTGTTCAGGACGCC 3'	
MKLC-2,	22mer	
5 '	GTGCTGCTCATGCTGTAGGTGC 3'	
MKLC-3,	23mer	
5 '	GAAGTTGATGTCTTGTGAGTGGC	3 '
Heavy Cl	hain Primers:	
IGG2AC-	1, 24mer	
5'	GCATCCTAGAGTCACCGAGGAGCC	3 '
IGG2AC-	2, 22mer	
5 '	CACTGGCTCAGGGAAATAACCC 3'	
IGG2AC-	3, 22mer	
5 '	GGAGAGCTGGGAAGGTGTGCAC 3'	

### FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3' T T T A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3

Heavy chain forward primer

FIG. 15

SL002B 39 mer

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

 $\mathbf{T}$ 

G

A

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

 $\mathbf{T}$ 

A

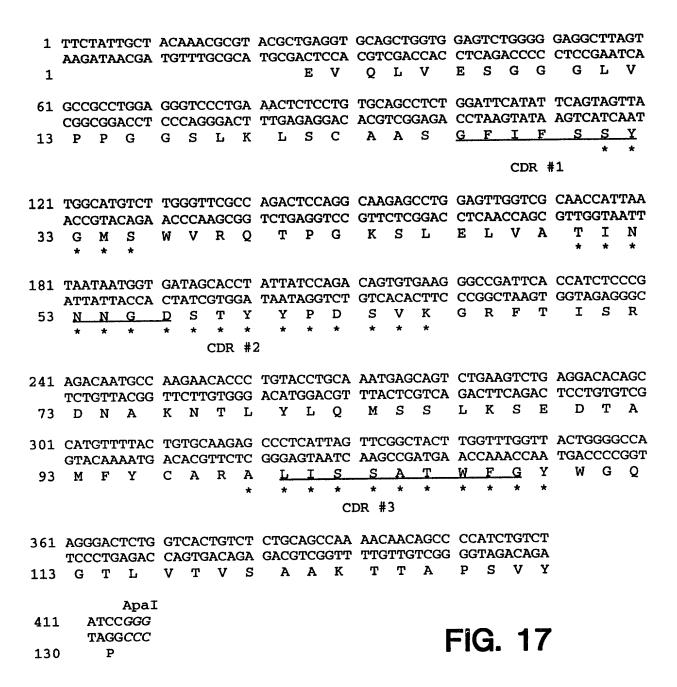
G

- GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC GTCCCAGTCG TACAGGIGIA GICAICCICT Ö Ŋ × AGTTTTTAAG Ŀ × Ø CTGTAACAGT ACTGTGTCAG Ø
- TGTCTTTGGT ACAGAAACCA ĸ Ø 61 GTCACCTGCA AGGCCAGTCA GAATGTGGGT ACTAATGTAG CCTGGTATCA TGATTACATC GGACCATAGT Ø CTTACACCCA N V G \* \* CDR #1 CAGTGGACGT TCCGGTCAGT 0 \* × υ E
- TCAGGGACTA AGTCCCTGAT М > GATTTACTCG TCATCCTACC GGTACAGTGG CTAAATGAGC AGTAGGATGG CCATGTCACC × × ₩ \* **CDR #2** ß Ϋ́Ι 121 GGGCAATCTC CTAAAGCACT CCCGTTAGAG GATTTCGTGA ď
- ACACGTCAGA TGTGCAGTCT Ø > ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT TGGGACAGAT TTCACTCTCA CCATCAGCCA S H Н FTLT Д H <sub>O</sub> CGCTTCACAG GCAGTGGATC CGTCACCTAG ט Ø GCGAAGTGTC Ö E ᄄ
- GTTCGGTCCT CAAGCCAGGA ტ TATAACATCT ATCCTCTCAC ATATTGTAGA TAGGAGAGTG PLT N N CDR #3 CTGTCAGCAA GACAGTCGTT O \* O + ပ GAAGACTTGG CAGACTATTT CTTCTGAACC GTCTGATAAA Σ Ω А 241 8
- GTAGAAGGGT CATCTTCCCA ACGGGCTGAT GCTGCACCAC CAACTGTATC TGCCCGACTA CGACGTGGTG GTTGACATAG Λ Д 더 A A P ď œ GGGACCAAGC TGGAGTTGAA CCCTGGTTCG ACCTCAACTT П Ж 团 301 101

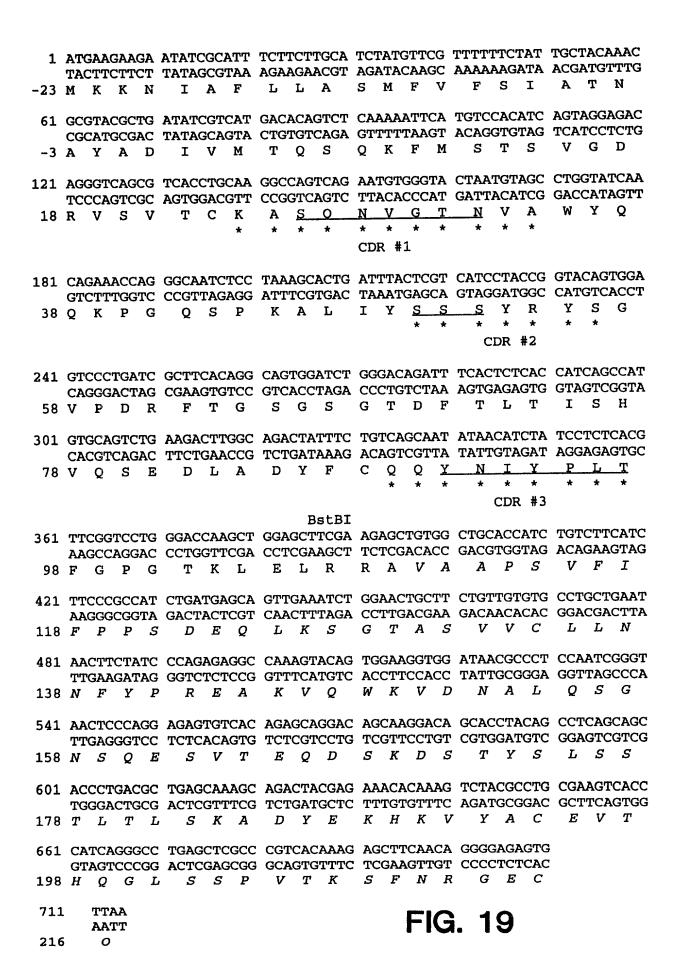
BstBI 361 CCATTCGAA GGTAAGCTT

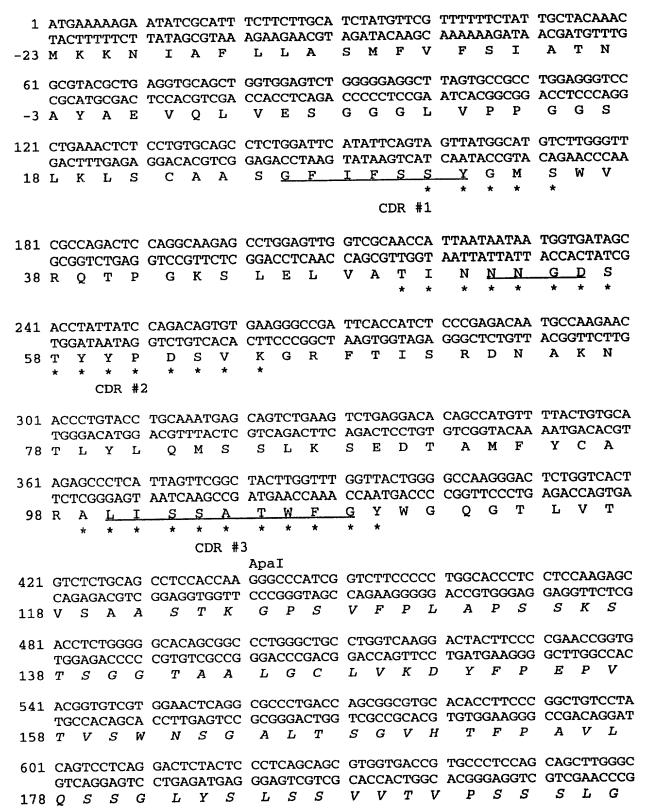
121 P F E

<u>-1G. 16</u>



VL.front	31-MER		
5' ACAA <u>ACGCGT</u> VL.rear 31-ME	ACGCT <u>GATATC</u> GTCATGACAG ER	3 '	
5' GCAGCATCAG	CTC <u>TTCGAA</u> GCTCCAGCTTGG	3 '	
VH.front.SPE	21-MER		
5' CCACTAGTAC	CGCAAGTTCACG	3 '	
VH.rear 33-MI	ER		
5' GATGGGCCC	TTGGTGGAGGCTGCAGAGACAGT	'G	3





**FIG. 20A** 

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K

721 GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT 218 V E P K S C D K T H T O

FIG. 20B

Light Ch	nain Primers:		
MKLC-1,	22mer		
5'	CAGTCCAACTGTTCAGGACGCC 3'		
MKLC-2,	22mer		
5'	GTGCTGCTCATGCTGTAGGTGC 3'		
MKLC-3,	23mer		
5'	GAAGTTGATGTCTTGTGAGTGGC	ا 3	
Heavy Chain Primers:			
5'	GCATCCTAGAGTCACCGAGGAGCC	3 '	
IGG2AC-	2, 22mer		
5'	CACTGGCTCAGGGAAATAACCC 3'		
IGG2AC-	3, 22mer		
5'	GGAGAGCTGGGAAGGTGTGCAC 3'		
	FIG. 21		

Programmer of the first state of

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
T T T T
A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

Heavy chain forward primer 6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3' T C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

 $\mathbf{T}$ 

Α

G

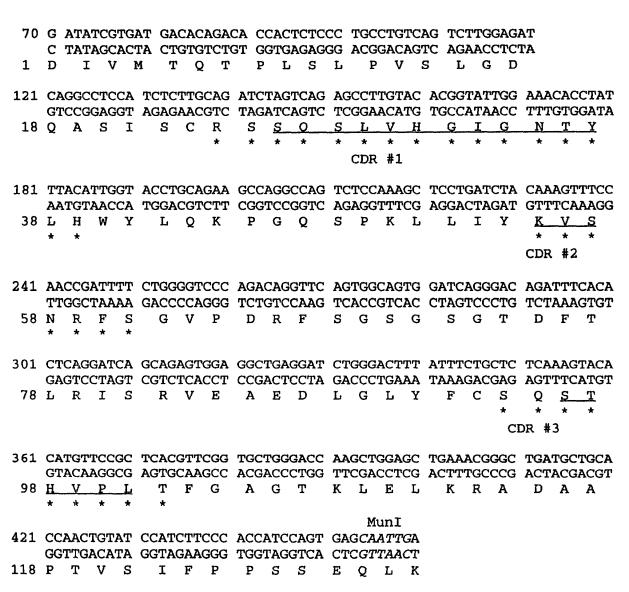


FIG. 24

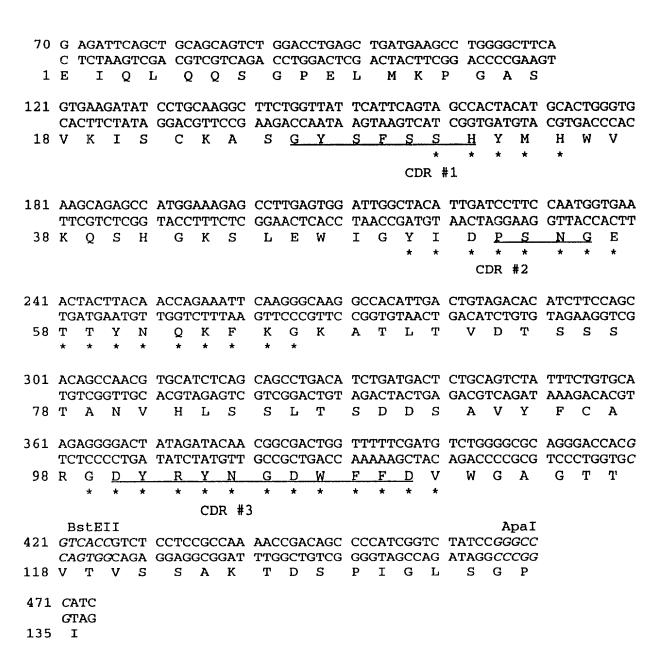


FIG. 25

5' CTTGGTGGAGGCGGAGGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

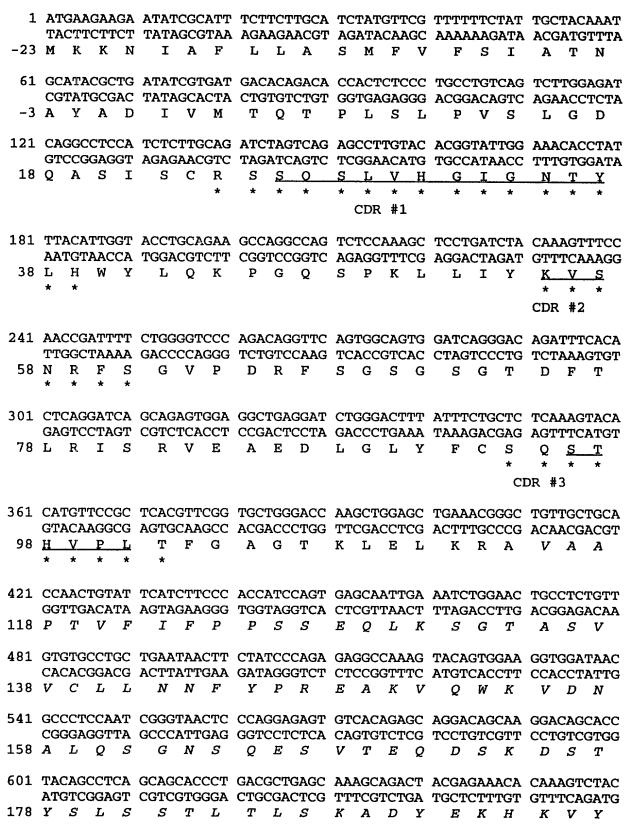
5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

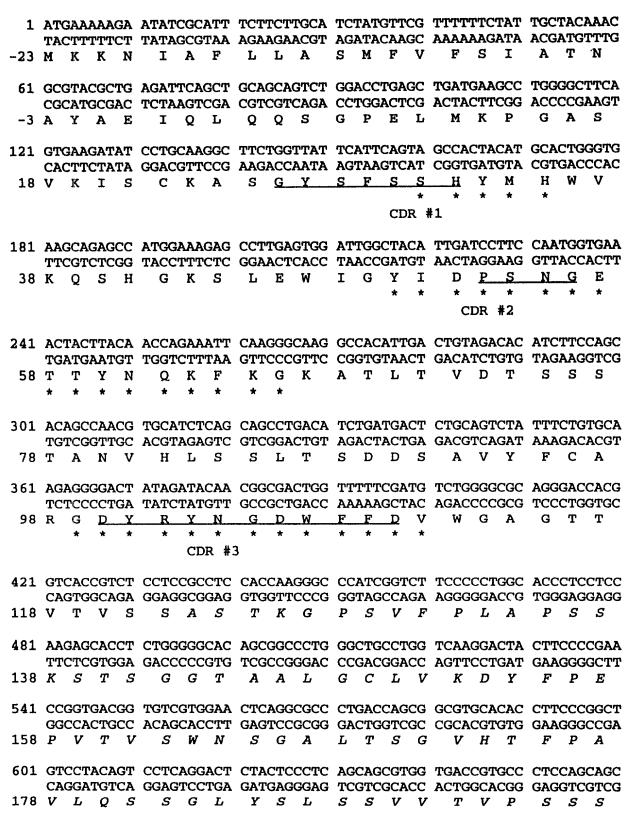
5' CTTGGTGGAGGCGGAGGAGACG 3'



**FIG. 27A** 

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA CGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT 198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAA CTCACAATT 218 E C O FIG. 27B



**FIG. 28A** 

AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG L G T Q T Y I C N N N H K P S N T K V D661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC 198

721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT  $218\ K\ V\ E\ P\ K\ S\ C\ D\ K\ T\ H\ T\ O$ 

### FIG. 28B

### Variable Light Chain Domain

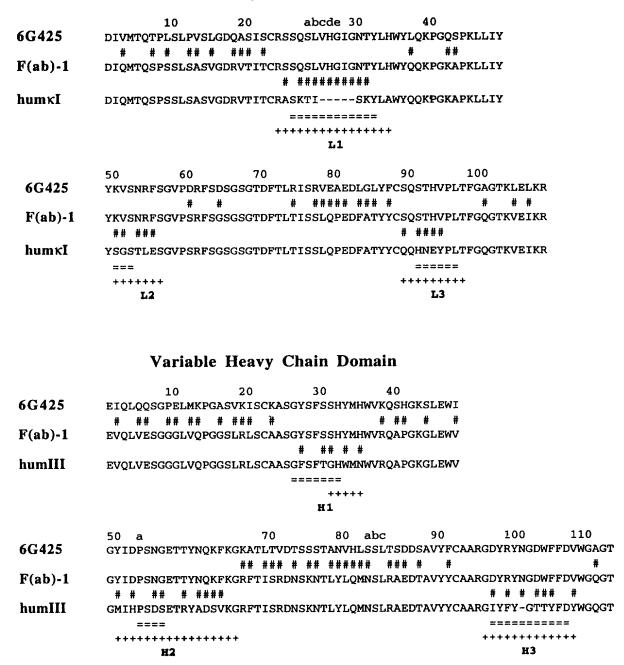
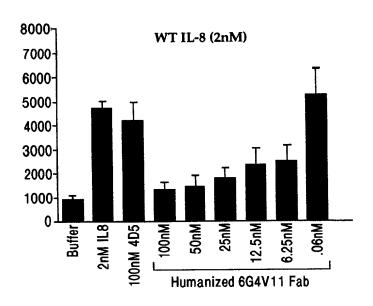


FIG. 29



**FIG. 30A** 

IC50~12nM

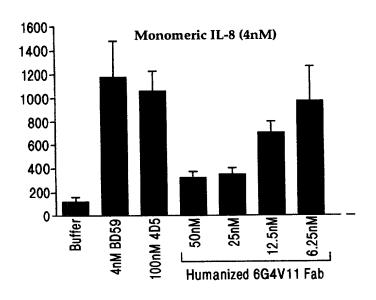
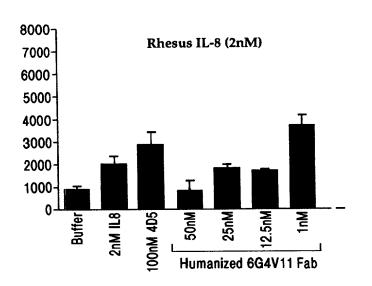


FIG. 30B

IC50~15nM



**FIG. 30C** 

IC50~22nM

## anti-IL-8 6G4.2.5V11 Light Chain Amino Acid Sequence of the humanized

LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY

# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFT**L**SRDNSKNT**A**YLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK  $\tt MKKNIAFLLASMFVFSIATNAYAEVQLV{\bf Q}SGGGLVQPGGSLRLSCAASGYSFSSHYMH$ VDKKVEPKSCDKTHT

# Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGSGDFDYEKMANANKGAMTENADENALQSDAKGKLDSVATDYGAAIDGFIGDVS GLANGNGATGDFAGSSNSQMAQVGDGDNSPLMNNFRQYLPSLPQSVECRPFVFSAGKPY **EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES** 

## FIG. 31A

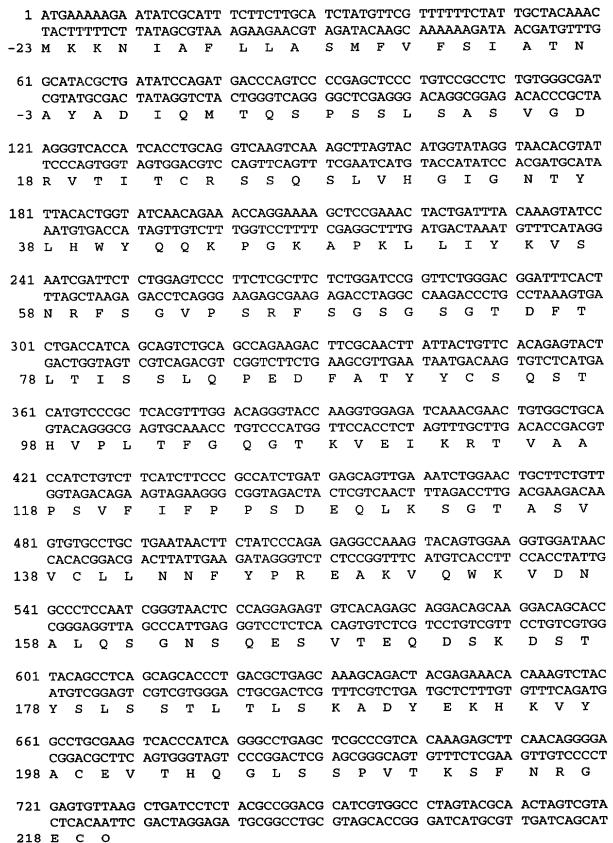


FIG. 31B

## Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY

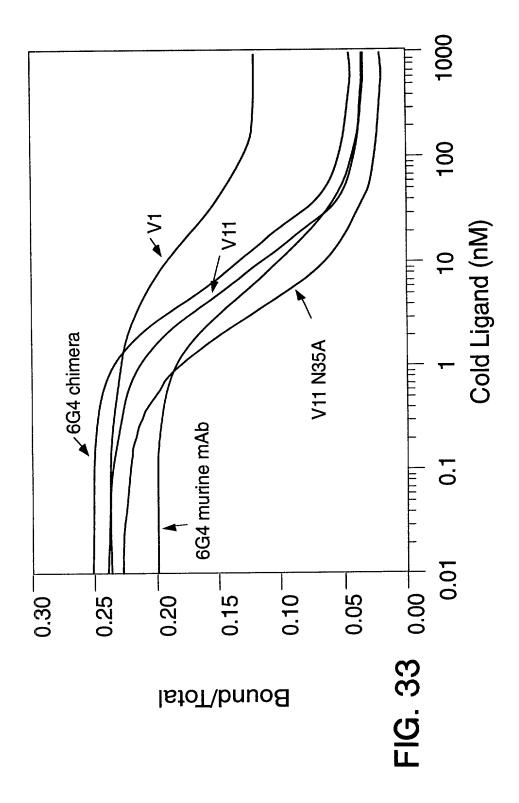
## Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

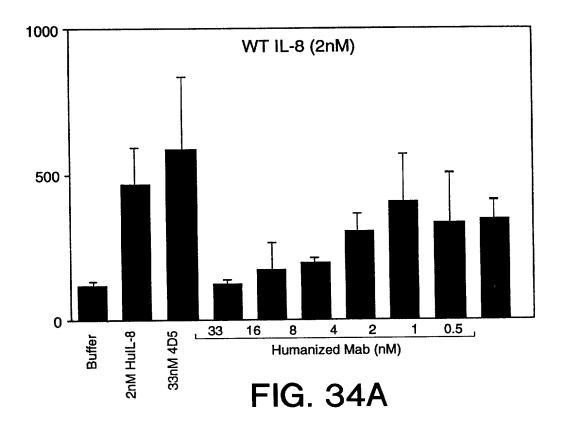
WVKQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT

FIG. 31C



F16.32





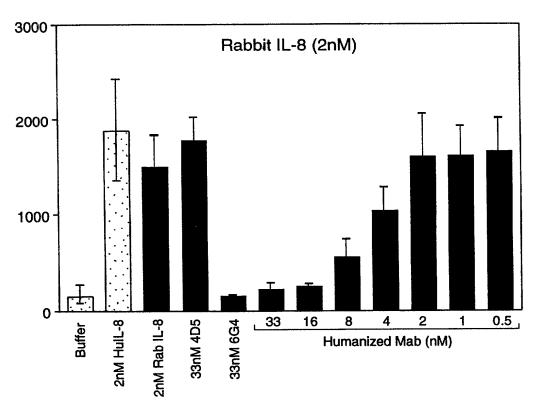
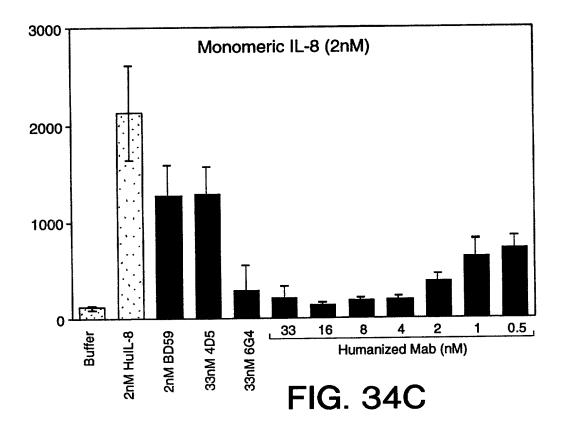
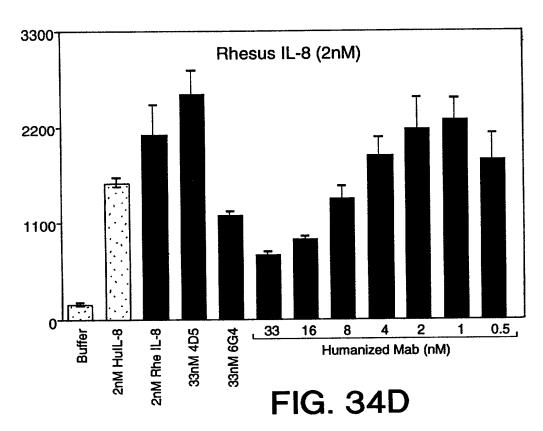


FIG. 34B





## Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIG**A**TY LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST

# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPE<u>LL</u>GGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER

FIG. 35

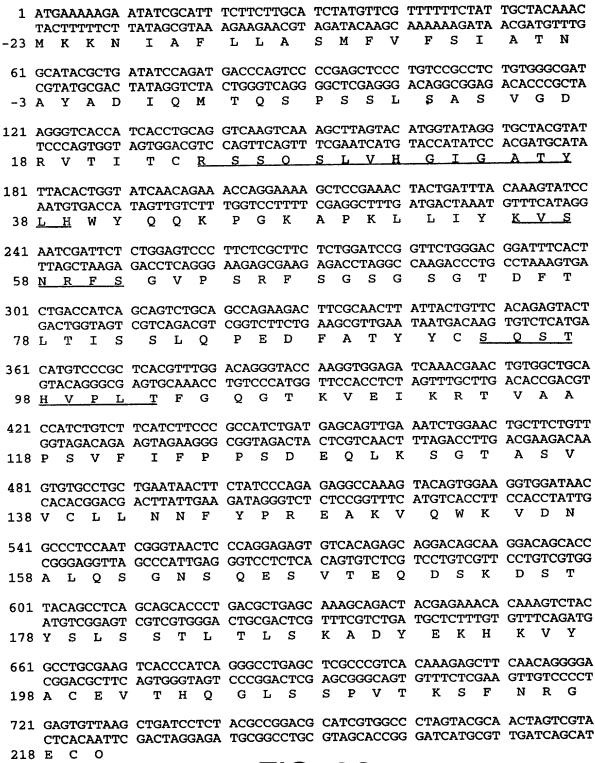
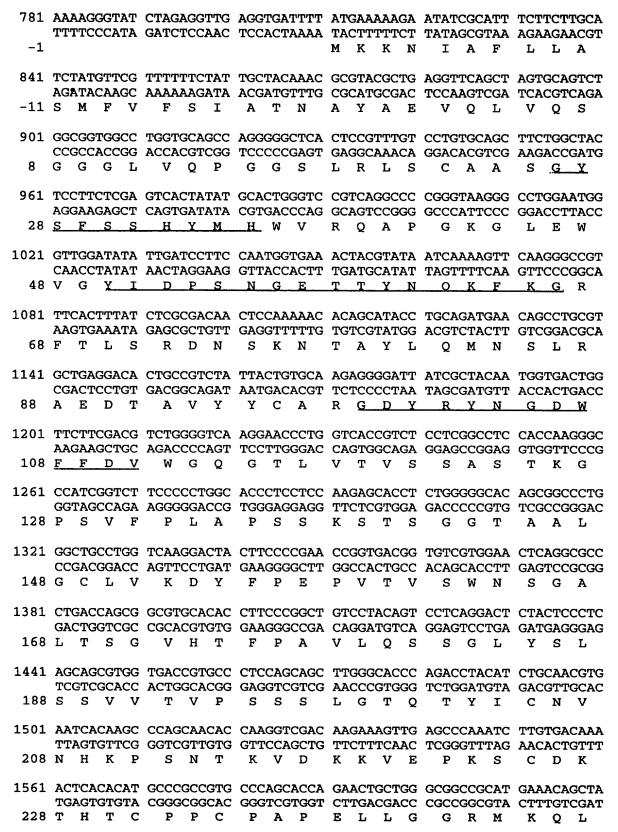


FIG. 36

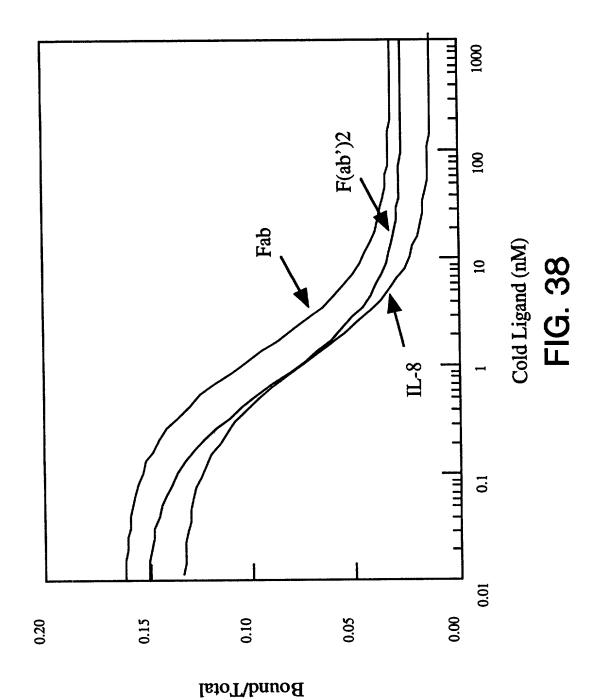


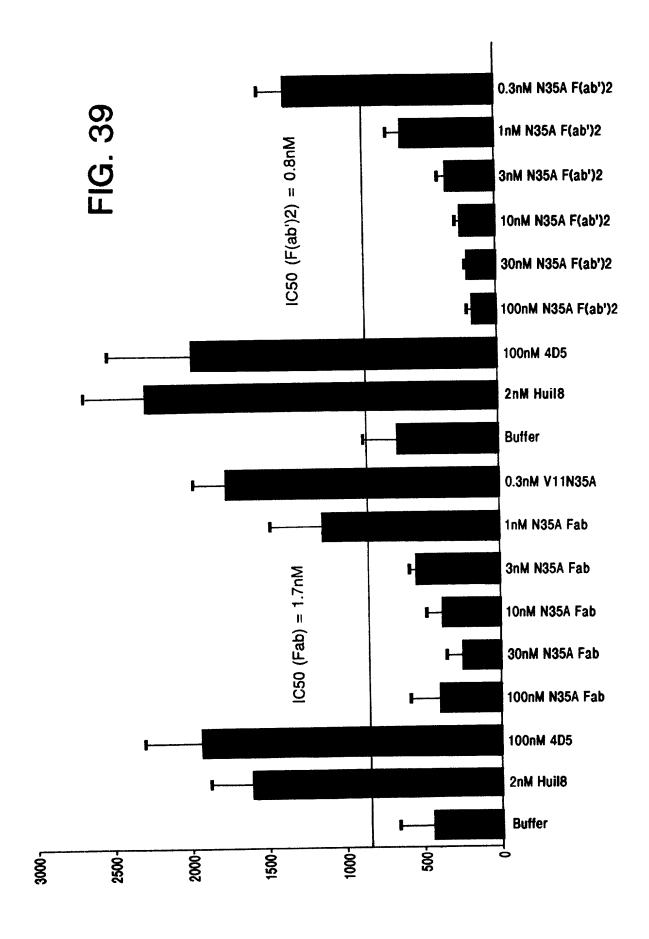
**FIG. 37A** 

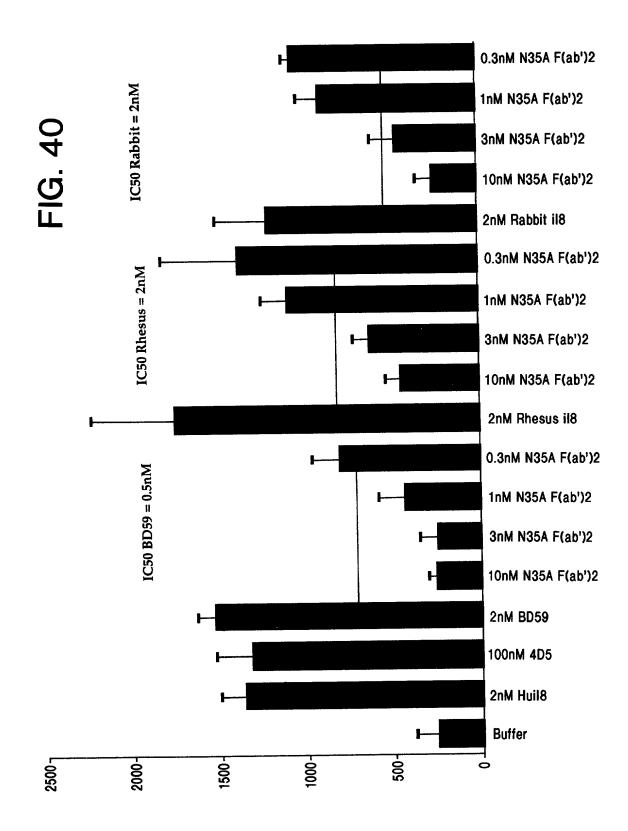
1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA CTCCTGTTCC AGCTTCTGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT 248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O

FIG. 37B







alui plei hindili mboli taqi 91 earl/ksp6321 . cac81 mboli hinfi AAGCTTGCCC AAAAGAAGA AGAGTCGAAT	sau3Al mbol/ndell[dam-] dpnl[dam+] acil dpnll[dam-] nspBll bcll[dam-] mnll ACCAACAGCG GTTGATTGAT CAGGTAGAGG	mnli foki sfani AAAGAAGTTA TTGAAGCATC CTCGTCAGTA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT	alui ssti saci hgiJII hgiJII hgiJII hgiJII ecll36II ecll36II mael bsiHKAI mael bmyI tru9I bfaI taqI msel maelII apol banII TTTTAATGTA GAATTCGAGC
ddeI tru bsrDI TCATTGCTGA GTTGTTATTT AGTAACGACT CAACAATAAA	msll harDl hhal/cfol attatcgrca ctgcaargc rcgcaararg raaragca cgccaratac cgccaratac	thal fnubli/mvni fnu4HI bsoFI bbvI maelI fnu4HI bbvI maelI fnu4HI bbvI maelI fnu4HI bbvI maelI bbvI bbvI bsoAlI aluI hhal/cfoI cGCA GCGATACGT GCGATACGT GCGATACGT AAAGAAGTTA	haeIII/pali mcri eagi/xmaIII/eclXI eae! cfri bsiEI ahdi/eam11051 tru91 maeIII bsmAI maeIII bsmAI mAGTGG GCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA ATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT
ecoRI pf1MI apoi bs11 1 GAATTCAACT TCCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG	bspMI hinPI hhal/cfoI mstI aviII/fspI hindIII 101 GAACTGTGTG GCGAGGTAGA AGCTTTGGAG CTTGACACAC GCGTCCATCT TCGAAACCTC	rsal hinpl hhal/cfol mnll cac81 haell csp61 sfaNl bsml 201 GGGCGCTGTA GCACTCCTGA CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT	ha mcr eag eae alu! cfr cfr bsi msel nspBil maeIII 301 AAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCACG TTTCAATTA GAAAGTTGT CGACAGTAT TCAACAGTGC

```
ddeI nlaIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            501 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCCGCCTCTG TGGGCGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            TAIGCGACTA TAGGICTACT GGGICAGGGG CICGAGGGAC AGGCGGAGAC ACCCGCTAIC CCAGIGGTAG IGGACGICCA GITCAGIITC GAAICAIGIA
Y A D I Q M I Q S P S S L S A S V G D R V I I I C R S S L V H
                                                                                                                                                                                                                                                                                                                           401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAAGAAT ATCGCATTTC TTCTTGCATC TATGTTCGTT TTTTCTATTG CTACAAACGC
                                                                                                                                                                                                                                                                                                                                        AGCCATGGGC CCCTAGGAGA GCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGCG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             hindIII csp6I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               aluI rsaI
                                                                                                                                                                                                                                                                                                                                                                           a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^{\circ}
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   bspMI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  sse8387I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                pstI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                scfI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  bstEII hphI bsgI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  bspMI
                                                                                                                                                                                                                                                                                                                                                                  IAFLLAS
                                                                                                                                                                                                                                                                                                                    sfaNI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      maeIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   hphī
                                                                                                                                                                                                                                                                                                                     Ilodm
                                                                                                                                                                                                                                                                                                                                                                      K K N
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         mpli
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           acil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         hgiAI/aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ec1136II
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsp1286
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsiHKAI
                                                                                                                                                                                                                                                                                                                                                                                                                                                          hgiJII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           tth1111/aspI banII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         bsrI aval aluI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             bmyI
                                                                                                                                                                                                                                                                                                                                                                                                                          sstI
                                                                                                                                                                                                                                                                                                                                                                                                                                           sacI
                                                                                                                                                                                                                                                                                                          hphI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             bsmFI
                                                                                                                                                                                                            mpol/ndeII[dam-]
                                                                                                                                                                                                                                           nlaIV paeR7I
                                                                                                                                                                                                                                                          kpnI cauII dpnII[dam-]
                                                                                                                                                                                             sau3AI taqI
                                                                                                                                                              xhoI
                                                                                                                                                                                                                                                                                                              bamHI avaI
                                                                                                                                                                                                                              dpnI[dam+]
                                                                                                                                                                                                                                                                              bstYI/xhoII
                                                                                                                                                                                                                                                                                              bani bsaJi alwi[dam-]
                                                                                                                                                                           mnlI
                                                                              xmaI/pspAI
                                              hpall
SCIFI
                                                               dsaV
               ncil
                               Idsm
                                                                                                              SCIFI
                                                                                                                                                                cauli
                                                                                                                                                                                bsaJI
                                                                                                smaI
                                                                                                                                                                                                avaI
                                                                                                                                ncil
                                                                                                                                                dsaV
                                                                                                                                                                                                                                                                                                              asp718
                                                                                                                                                                                                                              csp61
                                                                                                                                                                                                                                                                               hgiCI
                                                                                                                                                                                                                rsaI
                                                                                                                                                                                                                                                 nlaIV
```

SCIFI  mval  ecoRII  dsav  bstni aluI  bstni aluI  bspl(dam-)  clal/bspl06 pleI  bspl(dam-) hinfi  clal/bspl06 pleI  bstni apyl[dcm+]  ccatarccac ctacctartt acactggtat caacagaaaagc tccgaaacta ctgatttacaa tcgattctct ggagtcctt  ccatarccac gatgcataaa tgtgaccata gttgtctttg gtccttttgat gactttgat gactaaaatg ttcataggtt agctaagaga cctcaggaaa  c i g a i i i i i i i i i i i i i i i i i	Pash	styl bsaJI rsal csp61 nlalv kpn1 hgic1 mbol/ndell[dam-] fnu4HI mbolI ap718 dpn1[dam+] bsoFI bpuAl  maelI acc651 dpn1[dam-] bbvI bbsI mbolI  maelI acc651 carcrearca regeredace accacered racacered carcrearca carcrearca regeredate accacered racacered racacere
601 GGTATAGGTG CTACGT CCATATCCAC GATGCA	h h h h h h h h h h h h h h h h h h h	bsrBI acil bsmFI maeII 801 TGTCCCGCTC ACGTT ACAGGGCGAG TGCAA

Name
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1201 AGTĀCGCAAČ TAGTCGTAAA AAGGGTATCT AGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTC TTCTTGCATC TATGTTGTT TTTTCTATTG
TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
                                                                                                                                                                                                                                                                               1301 CTACAAAGGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC GATGTTTGCG CATGCGACTC CAAGTCGAT ACGTCAGAC GCCAACAGG ACACGTCGAA GACCGATGAG
                                                                               တ
                                                                                                                                                                                                                         alwNI[dcm-]
                                                                                                                                                                                                                                        fnu4HI
                                                                                                                                                                                                                                                                                                              CAA
                                                                                                                                                                                                                                                       DSOFI
                                                                                                                                                                                                                                                                     bbvI
                                                                                                                                                                                                             aluI
                                    mboli sfaNI
                                                                               ß
                                                                                 L
A
                                                                                 IAFL
                                                                                                                                                                                                                                                                                                                G
S
L
                                                                                                                                                                                                                          bsp1286
                                                                                                                                                                                                                                                                      banII
                                                                                                                                                                                                                                        apy1[dcm+] bsaJI bmyI
                                                                                                                                                                                                                                                       haeIII/pall apyI[dcm+]
                                                                                                                                          ecoRII
                                                                                                                                                                                                             dsav bstNI hgiJII
                                                                                                                                                                                                                                                                                                                VQPG
                                                                                                              SCLFI
                                                                                                                          mvaI
                                                                                                                                                       dsaV
                                                                                 K K N
                                                                                                                                                                                  fnu4HI
                                                                                                                                                                                                                            bstNI bsoFI
                                                                                                                                                                                                                                                                    Inqq
                                                                                                                                                                                               ecoRII
                                                                                                                                                                      SCLFI
                                                                                                                                                                                    mvaI
                                                                                                                                                                                                                                                                                                                  6
6
                                                                                                                                                                                                                                                                        acil hael
                            hphI
                                                                                                                                                                                                                                                                                                                                                SCLFI
                                         xbal muli muli
                                                                                                                                                                                                                                                                                                                 5 S Q
rmaI
               maeI
                             bfaI
                                                                                                                                                                                                                                                                                                                   VOLV
                                                                                                                                                                                                                                rmaI
                                                                                                                                                                                                                                             maeI
                                                                                                                                                                                                                                                           bfaI
                                                                                                                                                                                                                                                                       aluI
                                                                                                                                                                                                                                                            mluI csp6I mnlI
                                                                                                                                                                                                                                                                           ddeI
                                                                                                                                                                                                                                                                                                                     Y A E
                                                                                                                                                                                       bsiWI/splI
                                                                                                                                                                                                                fnuDII/mvnI
                                                                                                                                                                                                                                             bsh1236I
                                                                                                                                                                          rsaI
                maeI
                              bfaI
   rmaI
                                                                                                                                                                                                                                                                           afliii
                                                                                                                                                                                                                                  bstuI
                                             speI
                                              csp6I
                                                                                                                                                                                                                                                                                                                      H
```

FIG. 41E

ecoRII

SCLFI

xmaI/pspAI

SCLFI

SmaI

hpaII

dsaV

nciI mspI caull

bslI

mvaI

ncil dsav cauli

bslI

maeli snaBl hphi bsaAl ATGGTGAAAC TACGTATAAT TACCACTTTG ATGCATATTA	cac81 mnli cac81 ddel drdi GCCTGCGTGC TGAGGACACT GCCGTCTATT CGGACGCACG ACTCCTGTGA CGGCAGATAA L R A E D T A V Y Y	bmyI	asul panil apal styl asul styl asul mull bsaJI haeIII/pall eco01091/draII TCGCCTCCA CCAAGGGCCC AGCCGAGGT GGTTCCCGGG S A S T K G P 25chim2.fab2 ^
bsli sau3Al ideli[dam-] dpni[dam+] alwi[dam-] alwi[dam-] GATCCTTCCA CTAGGAAGGT		maeIII bstEII scrFI	II bsaJI bseRI c esp3I hphI bsmBI [dcm+] bsmAI 3T CACCGTCTCC A GTGGCAGAGG T T V S is from p6G4
bsaJI dsaV avaI bstNI bsaJI bslI sau96I apyI[dcm+] nlaIV sau96I haeIII/palI asuI ecol109I/draII haeIII/palI AGGCCCCG GGTAAGGGCC TGGAATGGGT TG TCCGGGGC CCATTCCCGG ACCTTACCCA AC	scfl pstl bsgl bspMI AGCATACCTG TCGTATGGAC		
bsaJI avaI bsaJI bsaJI sau96I sau96I avaII nlaIV asuI haeIII/palI nlaIV asuI ecool091/dra iGGGTCCG TCAGGCCCCG GGT	thal fnuDII/mvnI bstUI bsh1236I nruI CACTTTATCT CGCGACAACT CCAAAAACAC GTGAAATAGA GCGCTGTTGA GGTTTTTGTG		mael hinli ahali hphl bsrl mboll aatli CAATG GTGACTGGTT CTTCGACGT GTTAC CACTGACCAA GAAGCTGCA N G D W F F D V
bsaJI dsaV  avaI bstNI bsaJI bslI  taqI avaII nlaIV sau96I mboL/r  paeR7I asuI ecol1091/draII haeIII/palI  avaI maeIII bsrI ecol1091/draII dpnIII  1401 CTTCTCGAGT CACTATATGC ACTGGGTCCG GGTAAGGGCC TGGAATGGGT TGGATATATT  GAAGAGCTCA GTGATATATATATATATATATATATATATATATATATA	thal fundi/mvni haelii/pali bstui sau96i bshl236i asuI nrul 1501 CAAAAGTTCA AGGCCGTTT CACTTTATCT CGCGACAACT CCAAAAACAC GTTTTCTG GTTTTTGTG 62 Q K F K G R F T L S R D N S K N T		maell/e hinll/e ahall// maelli tagi hphi bsri mboli aatii 1601 ACTGTGCAAG AGGGATTAT CGCTACAATG GTGACTGGTT CTTCGACGTC TGACACGTTC TCCCCTAATA GCGATGTTAC CACTGACCAA GAAGCTGCAG 96 C A R G D Y R Y N G D W F F D V

## FIG. 41F

SCLFI

hphi mspi hpali cfr101/bsrFi bsaWi tth1111/aspi +] bsli agei maelli AAGGACTACT TCCCCGAACC GGTGACGGTG TTCCTGATGA AGGGGCTTGG CCACTGCCAC	ddel fnu4HI mnli plei bsoFi maeIII mnli eco811 hinfi ddel hphi bsp1286 CCTACAGTCCT ACTCCCTCAG CAGCGTGCCT GGATGTCAGG ACTCCTCAG CAGCGTGCTC ACGTGCCCT GGATGTCAGG ACTCCTCAGA TGAGGGAGTC GTGCACCAC TGGCACGGA L Q S G L Y S L S S V V T V P S  t aqi hgiJII sali bsp1286 styl hincil/hindii bmyi bsaJi acci banii maeIII bsaJi acci banii maeIII Sali AGCAACACCA AGGTCGAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC TCGTTGTGGT TCAGCTGTT CTTTCAACTC GGGTTTAGAA CACTGTTTTG S N T K V D K K V E P K S C D K T
scrFI mval scrFI mval ecoRII dsaV bstNI ecoNI sau96I dsaV haeIII/palI bstNI fnu4HI fnu4HI bstNI aciI apyI[dcm+] bsp1286 asuI bsoFI bmyI nspBII bsaJI bsvFI bmyI nspBII bsaJI bvoFI ccccGGGCACAG CGGCCCTGGG CTGCCTGGTC CCCCGGTGTC GCCCTGGTC GGGGCACAG CGCCCTGGG CTGCCTGGTC CCCCCGTGTC GCCCCTGGTC GGGGCACAG CGCCCTGGGCCCGGCCCGGGCCCGGGCCCGGCCC	
nlaIV hgiCI banI scrFI mvaI ecoRII dsay hgiAI/aspHI dsay hgiAI/aspHI apyI[dcm+] mnlI bsp1286 bpuAI apyI[dcm+] mnlI bmyI mnlI 1701 ATCGGTCTTC CCCTGGCAC CCTCCTCCAA GAGCACCTCT TAGCCAGAAG GGGGACCGTG GGAGGAGGTT CTCGTGGAGA 129 S V F P L A P S S K S T S	hinPI hial/cfoI hal/cfoI hall/aspHI hall/aspHI hall/acyI hall hall/bahI hall/bahI hall/bahI hall/bahI hall borI borI borI borI borI borI borI borI

#### FIG. 41G

									rmaI	maeI	bfaI	CTACCACCTA	GATGGTGGAT	Y H L	
							sapI	Ilodm	earI/ksp632I	bfaI tth1111/aspI	taqI aluI	GACAAGGIC GAAGAGCIAC ICICCAAGAA	CIGITCCAG CIICICGAIG AGAGGIICIT	D K V E E L L S K N	
fnu4HI	bsoFI	haeIII/palI	mcrI	eagI/xmaIII/eclXI	eaeI	cfrI	bsiEI	notI rmaI	fnu4HI maeI	bsoFI nlaIII bfaI	acil acil aluI mnlI	TCACACATGC CCGCCGTGCC CAGCACCAGA ACTGCTGGGC GGCCGCATGA AACAGCTAGA GGACAAGGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA		PELLGGRMKQLEDKVEELLSKNYHL	^junction between antibody and leucine zipper
								cac8I	nlaIII	nspI bsp1286	nspHI acil bmyI	TCACACATGC CCGCCGTGCC CAGCA	AGTGTGTACG GGCGGCACGG GTCGI	HIC PPCPAP	'junction between an

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scrFI  ddel nlaili	scrFI	Idsu	hpari	dsaV	CauII	aciI	fnu4HI	DSOFI	ACGCTCGGTT GCCGCCGGGC GTTTTTATT	TGCGAGCCAA CGGCGCCCG CAAAAATAA	
sphi ddei nlaili celli/espi blpi/bpul1021 hinPi nspi hhai/cfoi hhai/cfoi hinfi hindili eco47111 cac81 CTCTTACTTC ACGTTCTGA GTTTTTCGAA CAGCCCTCG CGATTCGTAC GCTG CTCTTACTTC ACGTTCTGA GTTTTTCGAA CAGCCCTCG CGATTCGTAC GCTG			rmaI	maeI	bfaI bsmFI	sau96I pleI	haeIII/palI	asuI hinfI	GGCCCT AGAGICCCTA	CCGGGA TCTCAGGGAT	
plei alui lindili bindili e oli GAGAATGAAG TGGCAAGACT CAAAAAGCTT GTCGGGGG CTCTTACTTC ACCGTTCTGA GTTTTTTCGAA CAGCCCCC CTCTTACTTC ACCGTTCTGA GTTTTTTCGAA CAGCCCCC	Idas	ddel nlaiii	cell1/espl	blpI/bpu1102I	hinPI nspI	hha1/cfo1			AGC GCTAAGCATG CGAC	ICG CGATICGIAC GCIG	R 0
pleI hinfI 01 GAGAATGAAG TGGCAAGACT ( CTCTTACTTC ACCGTTCTGA ( 52 E N E V A R L							aluI	hindIII	CAAAAAGCTT GTCGGGG	STTTTTCGAA CAGCCCC	K K L V G E
							pleI	hinfI	11 GAGAATGAAG TGGCAAGACT (	CICITACITC ACCGIICIGA (	52 ENEVARL

hpai nlaili clai/bsp106 tru91 tru91 tru91 hincil/hindii alui bspD1[dam-] msei acii msei msei bani 2201 GTTAACTCAT GTTTGACAGC TTATCATGA TAAGCTTTAA TGCGTAGTT TATCACAGTT AAATTGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC CAATTGAGTA CAAACTGTCG AATAGTAGCT ATTCGAAATT ACGCCATCAA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGGCACATA CTTAGATTG nlaIV taqı hindili tru9I mseI

haeIII/pall sau96I scrfl ncir rsal mspI mnli csp6I hpalI mspI dsaV bslI hpalI caulI ecoRV cfr101/bsrFI asul acil TCCGAACCAA TACGCCCATG AACGCCCATA	fnu4HI hinPI hgiAI/aspHI bsoFI hhaI/cfoI bsp1286 aciI haeIII/palI mstI bslI bsiHKAI mcrI eaeI aviII/fspI bmyI bsiEI cfrI TATGCGAACC CGTTCTCGGA GCACTGTCCG ACCGCTTTGG	mnli sau3Al mbol/ndeIl[dam-] dpnl[dam+] dpnl[dam+] dpnl[dam-] thaI thaI fnuDII/mvnI bstUI nlaIII bstUI nlaIII bsh1236I ATCGACTACG CGATCATGG CAGGACGCATC TAGCTGATGC GCTAGTACG CTGTGGG CAGGACGCACG TAGCTGATGC GCTAGTACG CTGTGGG CAGGACGCACG TAGCTGATGC GCTAGTACG CTGTGGG CAGGACACCT TAGGATGC GCTAGTACG CTGTGGGACACCT TAGGATGC GCTAGTACCT TAGGATGC GCTAGTACT TAGGATGC GCTAGTACCT TAGGATGC GCTAGTACT TAGGATGC GCTAGTACCT TAGGATGC GCTAGTACT TAGGATGC GC
haell] sau961 scrFI ncir rsaI mspI mnli csp61 hpall mspI dsaV bsl] hpall caull scfI CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGA	hinpI hhal/cfol mstl bsli sfaNI avill/fspl G ATGCAATTTC TATGCGCACC CGTT	sau3AI mboI/ndeII[dam-] dpnI[dam+] dpnII[dam-] thaI fnuDII/mvnI bstUI nlaIII bsh1236I CG CGATCATGGC GACCACCC GTCC
scfi crgraggcar gacarccgra	hinPI hhal/cfoldramai maei maei nhei flutHi haeii bsoFi eco47iii bbvi bfai cac8i cac8i TATGGCGTGC TGCTAGCGCTA	nlaIV TGGAGCCACT ACCTCGGTGA
sfaNJ scrFI mvaI ecoRII dsaV nlaIV bstNI mnlI hgiCI bsaJI hhaI/cfoI fokI banI maeIII fokI 2301 AATGCGTCA TCGTCATCCT CGGCACCGTC ACCTGGATG TTACGCGAGT AGCAGTAGGA GCCGTGGCAG TGGGACCTAC	maeIII sfaNI bsrI 2401 CCGACAGCAT CGCCAGTCAC GGCTGTCGTA GCGGTCAGTG	acil fnu4HI bsoFI acil bsrI cac8I 2501 CCGCCGCCA GTCCTGCTCG GGCGGCGGGT CAGGACGAGC GAAGCGATGA

### FIG. 41I

	cac81 sqr4 call hippi cac81 sgr4 haeli haeli haeli mbol/ndell[dam-] hqiJii haeli haeli/pali hpali hali/bsaHi ahali/bsaHi acil cac81 hphi mbol/[dam-] bpuli hali/cfoi cfr1 sfaNl cfr101/bsrFi acil cac81 hphi mboli[dam-] banii nlaili cfr1 sfaNl cfr101/bsrFi acil cac81 cac81 cac81 hphi mboli[dam-] banii nlaili cfr1 sfaNl cfr101/bsrFi acil cac81 hpli mboli[dam-] bmyl banii nlaili acii hinpi hinpi hai/cfoi daaV nlaiV	harl kası hinli/acyl hinli/acyl hinli/acyl hgiCi acii bsp1286 haeli bani bani ahali/bsaHi cac8l bsli acii acii haelli/pali GGCGCCATCT CCTTGCACGC ACCATTCCTT GCGCGCCGC TGCTCAACGG CCGCGGTAGA GGAACGTGC TGGTAAGGAA CGCCGCCCC ACGAGTTGCC
	hphi SC CGACATCACC G SG GCTGTAGTGG C hinPI hhal/cfoi nlalv	hari kasi hinli/acyi hgiCi haeli bani ahali/bsaHi GGCGCCATCT Co
hinPI hhaI/cfoI nlaIV narI kasI hinlI/acyI	ngici haeli bani ahall/bsaHi acii cac8i GCG GTTGCTGGCG CCTATATCC CGC CAACGACCGC GGATATAGC SCIFI ncii mspi hpall	bsli cauli sau961 haelll/pall nlaIV eael haelll/pall asuI bsaJI bsaJI ecol1091/draII cac81 bsli cfrI bsmFI GCAGGCC CCGTGGCCGG GGGACTGTT
hinpI hhal/cfoI hhal/cfoI nlaIV narI kasI hinlI/acyI hpaII hqiCI hpaII haeII naeI mspI	cac81 sgrAl cac81 sgrAl haelII/pall hpall eael hphl ahall/bsaHI cfrl sfaNl cfrl01/bsrFl a 2601 GTGGCGGCA TCACCGGCGC CACAGGTG CACCGGCCGT AGTGGCCGCG GTGTCCAC	bsli cauli nari sau961 haelil/pali kasi nlaIV eael hinli/acyl haelil/pali haeli asuI bsaJI bsaJI haeli cac81 bsli cfrI bsmFl ahali/bsaHl cac81 bsli cac8cccccccccccccccccccccccccccccccccc

mnli bsli bsri bbvi bsli hinfi hoga sectore sfani stani bsli alui bsli 2801 cctcaaccta ctactegect getectere controle con

pleI hinfI

ecoNI bslI

fnu4HI bsoFI

mspi hpaii bsaWI

fnu4HI  mspi hinpi  nael haeli  cfr101/bsrFi  cac81 eco47111  nlaIV bsoFi  hgiCI bbvI  bbsI nlaIII bani hpali hhal/cfoI mnll  cttatgactg tcttcttat catgcaactc gtacgacagc gctctgcgc  Gaatactgac agaagaaata gtacgttgag catcctgtcc acgccgtcg cgagaccgc	sau96I nlaIV avaII avaII acil tfiI ac8I mnlI maeIII bsmFI GCTTGCGGTA TTCGGAATCT TGCACGCCT CGCTCAAGCC TTCGTCACG GTCCCGCCAC	mcri eagl/xmalil/eclXi eael hinPi cfri hhal/cfol hgai nael fnu4Hi fnuDil/mvni cfr101/bsrFi bstUi cac81 acil hgai bgli nlalII haelII/pali maeli cac81 nrui bsh12361 foki haelI/pali cGCCGGCCACG CGCCGGTG CGCACGCGAGCCTC GCGCCGTAC CGCCGGAGCCTC GCCCGCAGCCTC GCGCCGTAC CGCCGCAGCCCCACG GCGCCCGACG CGCACGCCGACGCTC GCGCCCGACG CGCCGCACG GCGCCCGACG CGCCCGACGCCCCACG GCGCCCGACG CGCCCGACGCCCCCACGCACGCCCCCCCC
acil thai thai fuuDII/mvnI bstUI nlaIII acil mboII hinPI bcgI fnu4HI bbsI n hhal/cfoI bsoFI bbsI 2901 rGGGCGCGG GCATGATAT GCTCTTTTAT C ACCCGCGCC CGTACTGATA GCAGCGCGT GAATACTGACAAATA G	thal fnuDII/mvnI bstUI haeIII/palI acil bsh1236I sau3AI sau96I hinPI mboI/ndeII[dam-] avaII hhal/cfoI dpnI[dam+] acil tfiI asuI bpmI/gsuI[dcm-] dpnII[dam-] cac8I hinfI 3001 AGGACCGCTT TCGCTGGACGACGATGA TCGGACGATCATAGAATCT TCCTGGCGAA AGCGACCTCC CGCTGCTACT AGCCGTAGA	mcri eagl/xmall1/eclXI eagl/xmall1/eclXI eael hinPI cfrI hhal/cfol mspI bsiEl thal nael fnu4HI fnubl1/mvn cfr101/bsrFl bstUI haelI/pall hpall bsoFl bsh1236I spp1406I cac8I bglI nlalII haelII/pall 3101 CAAACGTTC GGCGAGAAGC AGGCCATTAT CGCCGCATG GCGGCGGCG GGCCCGGCTG GCGCGCGCGCGCGCGC

### FIG. 41K

bspMI scrFI mvaI ecoRII dsaV bstNI apyI[dcm+] bsmFI aluI alwI[dam-] TCCAGGCAGG TAGATGACGA CCATCAGGGA CAGCTTCAAG AGGTCCGTCC TCGAAGTTC	11 aJI hgiAl/aspHI bsp1286 bsiHKAI bmyI cac8I nlaIII nlaIII CTCGGCGAGC ACATGGAACG GGTTGGCATG	haeIII/palI sau961 bsoFI bsoFI ncil acil mspl mnlI hpaII mspl hpaII nlaIV dsaV naeI hqiCI caulI mnlI cacGCCCCCGCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
thal fnuDII/mvnI fnuDII/mvnI bstUI  I cac8I haeI msli sfaNI bshl236I haeIII/palI sfaNI fokI aciI cac8I nlaIII iGC ATCGGGATGC CCGCGTTGCA GGCCATGCTG	fnu4HI         sau96I         mnli         mnli           bsoFI         avaII         avaII         bsrI         bsrJ           thai         mbI/mvni         bsrI         sau3AI         mboI/ndeII[dam-]         bsaJI         hgiAI/aspHI           sau3AI bsh1236I         mboI/ndeII[dam-]         aciI         bsp1286           mboI/ndeII[dam-]         dpnI[dam+]         bsiHKAI           dpnI[dam+]         dpnI[dam+]         bsiHKAI           dpnII[dam-]         dcnII[dam-]         bsiHKAI           dpnII[dam-]         dcnII[dam-]         bsiHKAI	thal thal fuuDII/mvnI fuuDII/mvnI fuuDII/mvnI fuuDII/mvnI bstUI bstUI bsh1236I bsh1236I nlaIV mnll acil hgal acil nlaIII cerecegeg TrgcgTrcgc GTGCATGGAG GGAGGGCGC AACGCAGCGC CACGTACCTC
fnu bsc mboli aci tfil mspl hinfi hpall 3201 CCCATTATGA TTCTTCTCGC TTCCGGCG	fnu4HI bsoFI acil thai thai fnuDII/mvnI bstUI cac8I sau3AI bsh1236I mboI/ndeII[dam-] dpnI[dam+] dpnI[dam+] 3301 GATGGCTGG GGCTCTTACC AGCCTA CTAGCGAGGG CCGAGAATGG TCGGAT	fnu4HI bsoFI hinPI hhal/cfoI nlaIV narI kasI hinl1/acyI hgiCI haelI ahalI/bsaHI 3401 GATTGTAGGC GCGGCGGATA TGGAACAGAC CTAACATCCG CGGCGGGATA TGGAACAGAC

hgai thai acii fnuDii/mvni bstUi bsh1236i ATCCA TCGCGTCCGC	mspi hpali scrfi ncii dsav sau96i II cac8! II maei eco01091/drali cauli.bfal acii TGAGGACCCG GCTAGGCTGG	ddel nlaili GACCIGAGCA ACAACAIGAA CIGGACICGI IGIIGIACTI
flMI styl sli bsaji CAA CCCTTGGCAG AACATATCCA GTT GGGAACCGTC TTGTATAGGT	msp hpall scrFl scau3Al mbol/ndell[dam-] sau961 lam+] dam-] dam-] squII idam-] squII idam-] spl286 ppuMI maeI spl286 ppu	FI  maeII ddeI GCA AAACGTCTGC GACCTGAC
hinPI hhal/cfoI msti pflMI avill/fspI s bsmI bslI b sA ACTGTGAATG CGCAAACCAA CC	alI  dpnI[c Pl dpnI[l I/cfol hg nlaIII hs aviII/fs msl nsl n	cac81 bsoFI thaI thaI thaI hphI fnubII/mvnI fnu4HI tfiI bstUI hinfI bsh1236I maeII bbvI maeII GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAAGCGAC TGCTGCTGCA AAACGTCTGC
acil CCAATCAATT CTTGCGGAG GGTTAGTTAA GAACGCCTC	fnu4HI bsoFI bbvI GGGCAGCGTT CCCGTCGCAA	cac8I tha! tha! thal fnuDII/mvnI l bstUI fI bstUI maeII rCACCGATAC GCGAGCGAAC GF
hinPI hphI hphI mstI pflMI tfil pflMI acil bsmI bsmI bsmI bslI 3501 CTAACGGATT CACCACTCCA AGAATTGGAG CCAATCAATT CTTGCGGAGA ACTGTGAATG CGCAAACCAA GATTGCCTAA GTGGTGAGGT TCTTAACCTC GGTTAGTTAA GAACGCCTCT TGACACTTAC GCGTTTGGTT	fnu4HI thal hinPI that hinPI fnu4HI bsoFI bsoFI fnuDII/mvnI fnu4HI bstUI bsoFI cac8I hhal/cfoI bbvI aciI bsh1236I avaI bpmI/gsuI[dcm-] aciI sfaNI 3601 CATCTCCAGC AGCCGCAGG GGGGCATGTC GTAGAGGTCG TCGGCGTGCG GGGGTAGAG	cac81 thal thal thal thal hphI fnuDII/mvnI fnu4HI tfil bstUI bscFI bsrI hinfI bsh12361 maeII bbvI maeII ddeI nlaIII gCCCCAACG AATGACCAAT GCTTACTT AGTGGCTATG CGCTTGCTTG CTGCTGCTG TTTGCAGACG CTGGACTGT TGTTGTACTT gCCCCAACG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTTGCTTG CACTTGCTT ACTGGTATGTT
3501 CTA	3601 CAT	3701 CGC GCC

## FIG. 41M

```
apol bslI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 4001 CAACGIICCA GIAACCGGGC AIGIICAICA TCAGIAACCC GIAICGIGAG CAICCICIT CGIIICAICG GIAICAIIAC CCCCAIGAAC AGAAAIICCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  GITGCAAGGI CAITGGCCCG TACAAGTAGI AGICATIGGG CAIAGCACIC GIAGGAGAGA GCAAAGIAGC CAIAGIAAIG GGGGIACIIG ICITIAAGGG
                                                                                                                                                                                                                                                 TGGTCTTCGG TTTCCGTGTT TCGTAAAGTC TGGAAACGCG GAAGTCAGCG CCCTGCACCA TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC ACCAGAAGCC AAAGGCACAA AGCATTTCAG ACCTTTGCGC CTTCAGTCGC GGGACGTGGT AATACAAGGC CTAGACGTAG CGTCCTACGA CGACCGATGG
                                                                                                                                                                                                                                                                                                                                                                                                                               3901 CTGTGGAACA CCTACATCTG TATTAACGAA GCGCTGGCAT TGACCCTGAG TGATTTTTCT CTGGTCCCGC CGCATCCATA CCGCCAGTTG TTTACCCTCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                 GACACCTTGT GGATGTAGAC ATAATTGCTT CGCGACCGTA ACTGGGACTC ACTAAAAGA GACCAGGGCG GCGTAGGTAT GGCGGTCAAC AAATGGGAGT
                                                                                                                                                                                                                                    cac8I
                                                                                                                                                            fnu4HI
                                                                                                                                                                             bsoFI
                                                                                                                                                                                              bbvI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  nlaIII
                                                                                                                                                                                                                  sfani
                                                                                                                                                                                                                                    foki
                                                                                                                                                                                                                                                                                                                                                                                               bsrI
             mboI/ndeII[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                              acil
                                                                                                                                                             mroI bsaBI[dam-]
                                                                   dpnII[dam-]
                                                 dpnI[dam+]
                                  mamI[dam-]
                                                                                     bstYI/xhoII
                                                                                                          alwI[dam-]
                                                                                                                                                                                                                                accIII[dam-1
                                                                                                                                                                                                                                                                                                                                                         sfani
                                                                                                                                                                                                                                                                                                                                           fokī
                                                                                                                                                                                                  bspEI[dam-]
sau3AI
                                                                                                                                                                                                                                                                                                                                                                                              avall fnu4HI
                                                                                                                                                                                                                                                                                                                                                                               aciI
                                                                                                                                                                                                                                                                                                                                                                                                                 asuI bsoFI
                                                                                                                                            hpall
                                                                                                                                                                               bspMII
                                                                                                                                                                                                                    bsaWI
                                                                                                                             Idsm
                                                                                                                                                                                                                                                                                                                          acil
                                                                                                                                                                                                                                                                                                                                                        sau96I
                                                                                                                                                                                                                                                                                                                                           DSMFI
                                                                                                                                                                                                                                                                                                                                                                               nlaIV
                                                                                                                                                                                                                                       mslI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 mnlI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                fokI
                                                                                                                                                                                                                      hhaI/cfoI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    sfani
                                                                                                                                                                                                   fnuDII/mvnI hinPI
                                                                                                                                                                                                                                       haeII
                                                                                                                                                                                                                                                                                                                                                                                                                  ddeI
                                                                                                                                                                                                                                     bsh1236I
                                                                                                                                                                  acil
                                                                                                                                                                                                                      bstuI
                                                                                                                                                                                    thaI
                                                                                                                                                                                                                                                                                                                                                                                hhaI/cfoI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   maeIII
                                                                                                                                                                                                                                                                                                                                             cac8I
                                                                                                                                                                                                                                                                                                                                                                                                                 eco47III
                                                                                                                                                                                                                                                                                                                                                           hinPI
                                                                                                                                                                                                                                                                                                                                                                                                  haeII
                                                                                                                                                                                                                                                                                                                                                                                                tru9I
                                                                                                                                                                                                                                                                                                                                                                                                                   mseI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  dsaV nlaIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    psp14061 maeIII nspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Igan
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               hpall
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    cauli
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           SCIFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ncil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Idsm
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   bs1I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   \mathbf{bsrI}
                                                                                                                                                                                                         IIoqu
                                                                                                                                                                                                                          ppuAI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     maelI
                                                                                                                                                                                                                                            bbsI
                                                                                                                                                                                                                                                             3801
```

### FIG. 41N

cac8I
sau96I
tru9I haeIII/palI
mseI asuI

GGAATGIGCC ICCGIAGITC ACTGGITTGI CCITITITGG CGGGAATTGI ACCGGGCGAA AIAGICITCG GICTGIAAIT GCGAAGACCI CITIGAGITG 4101 CCTTACACGG AGGCATCAAG TGACCAAACA GGAAAAAACC GCCCTTAACA TGGCCCGCTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC bpmI/gsuI[dcm-] mseI acil bsli nlaili acil maelli sfani mnlI

thal

fnu4HI

hphI hphI fnuDII/mvnI fnuDII/mvnI hhal/cfol mnll bsh1236I bsh1236I bstul hinPI bstul thaI **bsof**I acil bbvI nspBII aluI IInad fnu4HI **bsoFI** bcgI bbvI aluI mslI asp700 hinfI tfiI XmnI fnuDII/mvnI bsh1236I aluI hgaI fokI aciI bstul thaI

4201 GAGCIGGÁCG CGGAIGAACA GGCAGACAIC IGIGAÁICGC IICACGACCA CGCIGAIGAG CITIACCGCA GCIGCCICGC GCGIIICGGI GAIGACGIG CICGACCIGC GCCIACTIGI CCGICIGIAG ACACIITAGCG AAGIGCIGGI GCGACIACIC GAAAIGGCGI CGACGGAGCG CGCAAAGCCA CIACIGCCAC

esp31
bsmB1
bsmB1
bsmA1
msp1
fnu4H1 hpa11
bsoF1 scrF1
bbvI nci1
nla111 dsaV

GGCGCGTCAG CGGGTGTTGG TITIGGAGAC IGIGIACGIC GAGGGCCTCI GCCAGIGICG AACAGACAII CGCCIACGGC CCICGICIGI ICGGGCAGIC CCGCGCAGIC GCCCACAACC 4301 AAAACCICIG ACACAIGCAG CICCCGGAGA CGGICACAGC IIGICIGIAA GCGGAIGCCG GGAGCAGACA AGCCCGICAG

acil

hinPI nspBII

hhaI/cfoI

drdI

Cauli

acil

fokI dsaV

aluI

caull

Idsu

nspHI aluI bslI

maeIII

sfani

hpall

Idsm

bsh1236I

fnuDII/mvnI bstUI aciI

hgaI

SCIFI

nciI

thaI

### FIG. 410

hgiAl/aspHI bspl286 bsiHKAI [ bmyI ndeI apaLl/snoI alw441/snoI AGAGTGCACC	foI mcrI bsiEI CGGTCGTTCG GCCAGCAAGC	bsli cac81 haeIII/pal1 haeI AGGCCAGCAA	mnlI CAGAGGTGGC GTCTCCACCG
maeli sfani sfani bsp1286 lii hgial/a saAl bst11071 tru91 bsoFi rsaI apall/s ACGTAGCGAT ACCGCACTC ATACTATGCGG CATCAGACCA GATTGTACTG TACAGAGCG TACACGTGGC TACACGAGG TATACAGAGC TAGATACGCC GTAGTCTCGT CTACACGTGG	hinPI hhaI/c fnu4HI bsoFI I bbvI ICGCTGCGCT	III [ II h ICTGAGCAAA A	aI dI ACGCTCAAGT IGCGAGTTCA
sfaNI fnu4HI bsoFI acil GCGG CATCAGAGC		nla] nspi nspi afii] A GGAAAGAACA 1	hg dr I taqI C ACAAAAATCG ; G TGTTTTAGC ;
sf fnu4H tru9I bsoFI mseI aciI TT AACTATGCGG	mboll earl/ksp6321 sapl hinPl hhal/cfol haell acil mnll AGGGGCTCTT CCGCTTCCTC TCCGCGAGAA GGCGAGGGG	GGATAACGC	sfani T GACGAGCATC
bstll071 t acci bsri n GT ATACTGGC! CA TATGACCG4		tfiI hinfI CA CAGAATCAG	cel acil  creccert recatager ecececer  gaccecaaaa agerareea geegegege  FIG. 41P
acil s AT AGCGGAGT	sfaNI acil AA ATACCGCATC TT TATGGCGTAG	acil GGCGGTAATA CGGTTATCCA CCGCCATTAT GCCAATAGGT	n13 TT TCCATAGGG AA AGGTATCC
고 및 엑	I CG TAAGGAGAAA GC AITCCICTIT		
AIII bsr tth111 TGACCCA	acii sfaNI TGAAATACCG CACAGATGCG ACTTTATGGC GTGTCTACGC	aluI AG CTCACTCA	thal fnuDII/m bstUI bsh12361 acil fnu4HI bsoFI ca haeIII/palI haeGCCGCGTTG
	acil acil sfaNI ATATGCGGTG TGAAATACCG CACAGATGCG	acil bsrBi c8i GA GCGGTATC	bsli m+] ili V GCGTAAA TGGCATTT
4401 CGGGTGTCGG GCCCACAGCC	acil 4501 ATATGCGGTG TATACGCCAC	fnu4HI bsoFI acil fnu4HI bsoFI b bbvI cac 4601 GCTGCGGCG	scrFI mvai ecoRII dsaV bstNI b apyI[dcm+ haeIII/paiI haeI nlaIV 4701 AAGGCCAGGA AC TTCCGGTCCT TG
4	4	4	4

	acil ACCTGTCCGC FGGACAGGCG	hgiAl/aspHI bsp1286 bsiHKAI bmyI apaLl/snoI alw441/snoI TGTGCACGAA	alwNI[dcm-] nu4HI soFI HI I maeIII bvI bsrI CA GCCACTGGTA	hinPI hhaI/cfo
	ecoRII dsaV dsaV dsaV bstNI bstNI bstNI apyl[dcm+] bssSI apyl[dcm+] bsaJI aluI mnll hhal/cfoI bsoFI bsaWI acit daaacccGaC aggaCTATACCAGG CGTTTCCCCC TGGAAGCTCC CTCGTGCGCT CTCCTGTTCC GACCTGCCG CTTACCGGAT ACCTGTCGCG CTTTGGCTG TCCTGATATT TCTATGGTCC GCAAAGGGGG ACCTTCGAGG GAGCACGCGA GAGGACAAGG CTGGACGCCTA TGGACGGG	HA	fnu4HI bsoFI  acil hinPI maeIII  mcI bbvI  bsiEI hhal/cfoI hpaII  bsiEI hhal/cfoI hpaII  cccccGTTC AGCCCGACC CTGCGCTAACT ATCTCTTTGA GTCAACCCG GTAAGACACG TGAATAGCGG TGAATAGCGG TGACCGTCGT  GGGGGCAAG TCGGCTACATTGA TAGCAGAACT CAGGTTGGGC CATTCTGTGC TGAATAGCGG TGACCGTCGT  alwwl[dcm-]  bsoFI  cauli  bsoFI  cauli  bscCCCGTCACCCG GTAAGACACC GTAAGACACC ACTGGCACACCGCACACCACCACCACCACACACACACACA	
	acil msp fnu4HI bsoFI c GACCCTGCCG C	GTTCGCTCCA	ACTTATCGCC	rmal mael bfal
	bsli si hhal/cfol srcccr crcrgrrcc	scfI ddeI CGCTGTAGGT ATCTCAGTTC GGTGTAGGTC GTTCGCTCCA AGCTGGGCTG GCGACATCCA TAGAGTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC	mspl hpall crFl cil saV aull ccG GTAAGACACG	bsli haeIII/pall aeI
	hinPI cm+] bssSI aluI mnlI hhal AAGCTCC CTCGTGCGC	ddel GT ATCTCAGTT CA TAGAGTCAA	mspl hpal scrfl ncil plel dsav hinfl caull GA GTCCAACCCG	bsli haeIII haeI
scrFI	apyl[dcm+] bsaJl aluI ccc rgGAAGCT		II B CT ATCGTCTTG GA TAGCAGAA(	
н	ecoRII dsav dsav bstNI bstNI apyl[dcm+] k CCAGG CGTTTCCC	foI aluI FC TCATAGCT AG AGTATCGA	HI  T  MaeIII  hinpI mspI  bsaWI  hhal/cfoI hpaII  GCGCCTTA TCCGGTAACT	acil scfl
SCLFI MVaI	ecorii dsav bstni apyi [d AA AGATACCAGG	hinPI hhal/cfoI haeII G TGGCGCTTTC	fnu4HI bsoFI nspBII acii hinPI I bbvI EI hhaI/cf CCG CTGCGCCTT	
	AC AGGACTAT? FG TCCTGATA!	hinPI hhal/cfoI haeII aluI CTTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATAGCTCA GAAAGAGGGA AGCCCTTCGC ACCGCGAAAG AGTATCGAGT	fnu4 bsoF nspBII acil j mcrI bbvI bsiEI c AGCCCGACCG CPC	Ilam
	)1 GAAACCCG2 CTTTGGGCT	hinPI hhal/cfoI haeII aluI 4901 CTTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATAGCTCA GAAAGAGGGA AGCCCTTCGC ACCGCGAAAG AGTATCGAGT	1 CCCCCGTT	Z KEER KUU KEER KEER
	48(	490	200	

## FIG. 41Q

mnli acti scfi hal/cfoi scfordacin scfi hal/cfoi scfordacin scfordacin scfordacin hal/cfoi scrotagarge targrades greenedes scrotagarge acadastre grandes grandes scrotagarge scrotagarge scrotagarge scrotagarge scrotagarge scrotagarges scrot

mspl hpall sau3Al mbol/ndell[dam-] dpnl[dam+] dpnl[dam-] acil acil acil cac8l AGTTGGTAGC TCTTGATCG GCAAACAAAC CACCGCTGGT TCCCCACCAA AAAAACAAAC GTTCGTCGTC	tru9I nlaIII mseI rcaI maeII bspHI ACGTTAAGG ATTTGGTCA TGCAATTCC TAAAACCAGT	maeIII TAAACTTGGT CTGACAGTTA ATTTGAACCA GACTGTCAAT
II acil rggr agcggrggrr ri acca rcgccaccaa aa		AAAG TATATATGAG 12 TITC ATATATACTC A1
mspl hpall sau3Al mbol/ndell[dam-] dpnl[dam+] alw1[dam-] acil gATCCG GCAAACAAAC CTAGCC CGTTTGTTTG GTGGCGAC	JAI   JudeII[dam-]   JudeII[dam-]   JudeII[dam-]   Jul[dam-]   Jul[dam-]   Jul[dam-]   Jul[dam-]   Jul[dam-]   Jul[dam-]   JudeI   J	tru9I mseI ahaIII/draI AGTTTAAAT CAATCTAAAG
mspI hpaII sau3AI mbol/ndeII[dpn+] dpnI[dam+] aluI alwI[dam-] gGTAGC TCTTGATCG GCAA	sau3AI sau3AI mbol/ndeII[dam-] mboII[dam-] dpnI[dam+] I[dam-] dpnI[dam+] -] dpnI[dam+] -] dpnI[dam-] -] dpnI[dam-] I alwI[dam-] I alwI[dam-] KGAA GATCCTTTGA TCTTTTCTAC GOOTT CON CONTACT CONTACT CON CONTACT CONTACT CON CONTACT CONTACT CON CONTACT CON CONTACT CON CONTACT CON CONTACT CON CONTACT CONTACT CON CONTACT CONTACT CON CONTACT CONTACT CON CONTACT CON CONTACT CON CONTACT CON CONTACT CON CONTACT CONTACT CON CONTACT CONTACT CON CONTACT CON CONTACT CON CONTACT CONT	sau3AI mbol/ndeII[dam-] uI dpnI[dam+] el tru9I mm-] mseI dpnII[dam-] alwI[dam-] tru9I stYI/xhoII mseI nI ahaIII/draI AI ahaIII/draI AGAAAATTT AATTTTTACT
T TCGGAAAAG A AGCCITITIC	sau3AI m mboI/ndeI sau3AI m mboI/ndeI dam-] d dpnI[dam+] dpnI[dam+dpnI[dam+] dpnI[dam+strl/xhoII alwI[dam-alwI[dam-] bstrl/xhoII gG ATCTCAAGAA GATCCTTGC CC TAGAGAAAC	sau3AI rmaI rmaI hphI dpnI[dam+] mboII[dam-] sau3AI maeI tru mboI/ndeII[dam-] mse dpnI[dam+] dpnII[dam-] dpnII[dam-] bstYI/xhoII alwI[dam-] bfaI AAAAAGGATC TTCACCTAGA TCCTTTTA
maeIII eco571 bsrI 5201 TCTGCTGAAG CCAGTTACC AGACGACTTC GGTCAATGG	sau3Al mbc mbol/ndeII[ hinPI sau3Al mbol/ndeII[ hhal/cfol mbol/ndeII[dam-] dpr thal dpnI[dam+] dpnI[dam+] fuuDII/mvnI dpnI[dam+] dpnI[dam+] bstUI bstYl/xhoII alwI[dam-] bsh1236I alwI[dam-] bstYl/xhoII sau1Gam-] TAATGCGCG GAAAAAAAGG ATCTCAAGAA GATCCTTTGA	sau3Al  mbol/ndell[dam-]  rma!  hphi dpnl[dam+]  sau3Al mael tru9!  mbol/ndell[dam-] msel  dpnl[dam+] dpnl[dam-] tru9!  bstXl/xhoIl bstXl/xhoIl msel  alw[[dam-] bfal ahaIll/dra! ahaIll/dra!  s401 TGAGATTATC AAAAAGGATC TTCACCTAGA TCCTTTTAAA TTAAAAATCA AGTTTTAAAG TATATATGA GACTGTCAATAAAAATCA AGTTTTAACT TCAAAAATTTA GTTAGATTC ATATATACTC ATATATACTC ATATATACTC ATTTGAACCA GACTGTCAATA
5201	5301	5401

mnli sol ccaargctra atcagtgagg cacctarcte aggaretge ctatteget catccaragt tgeetgacte eccgreget agaractae garacggagg garacgaag garacgaag garacgaag garacgaag ctargeete cargerete aggrangaat tagteactee grggaragae recetagaea garaaageaa grageratea acgaactgag gggeageaca tetatrgarg etargeeere FIG. 41R

hinfI

mbol/ndeII[dam-] dpnI[dam+]
dpnII[dam-]

sau3AI

nlaIV hgiCI banI

tru9I

bsai bpml/gsul[dcm-] sau961 fnu4H1 fnuDII/mvnI mspl hpail nlaIV bsoFI bstUl cfr10I/bsrFI cac81 asu1 hhal/cfoI asu1 bbvl aci1 hph1 nlaIV 5601 GGCTTACCAT CTGGCCCCAG TGCTGCAATA TAGGCCTCA GTCTGGCCTCA GTCTGGCCTCA GTCTGGCCTCA CGGCTCGAGGT CTAAATAGTC GTTATTTGT CGGTCGGCTC TCCGGCTCG TGCTGCTCA TATGGCGCTC TGGGTGCGAGGT CTAAATAGTC GTTATTTGT CGGTCGGCTC TCCGGCTCG	ncil mspl hpall rmal hpall rmal tru9l dsaV mael msel caull bfal bsrl msel avill/fspl TATTAATTGT TGCGGGAAG CTAGAGTAAG TAGTTCGCCA ATAATTAACA ACGCCCTTC GATCATTC ATCAAGCGGT CAATTATCAA	cac81 scf1 pst1 pst1 fnu4HI bsoFI bsoFI bsrDI bsg1 sfaNI maeIII alw1[dam-] alu1 hpaII bsrDI bsg1 sfaNI acaccaccac accaccaccaccaccaccaccaccaccac
mspi hpali bgli cac8i A GCCAGCCGA	tru9I bsrI mseI CCA GTTAATAGT	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] maeI GATCAA GGCGAGTTA
l ag caataaacc ic gitaitige	bs ag tagticge ic atcaageg	V sau3AI mbol/n dpnI[d dpnII[ cc caacgarcaa
bpmI/gsuI[dcm-] :I I/bsrFI aIV :CTCCA GATTTATCA	rmal mael bfal alul AG CTAGAGTA	nlaIV mspI bsaWI aluI hpaII CAG CTCCGGTTC
bpmI/gs mspI hpaII cfr10I/bsrFI hphI nlaIV crc ACCGGCTCCA G	scrFI ncil mspI hpaII tru9I dsaV mseI cauII aseI/asnI/vspI ATTAATTGT TGCCGGGZ	TGG CTTCATT
bsmAI bsaI thaI fnuDII/mvnI bstUI bsh1236I ciI	tru9I rI mseI aseI/a AGTC TATTAAT	GTCG TTTGGTA
bs thal thal [ fnuDI bstUI cDI bsh12 AATG ATACGGGA	sau96I avaII aciI fokI asuI aciI fokI 5701 GCAGAAGTGG TCCTGCAACT TTATCCGCCT CCATCCAGTC	maelli figic acgete acag igcgag
bsrl fnu4HI nlaIV bsoFI haeIII/palI bsrDI asuI bbvI GGCCCCAG TGCTGCAAT	ac LAACT TTATCC	BI msli sfani kGGCA TCGTGG
bs sau96I nlaIV haeIII asuI CCAT CTGGCCC	sau96I avaII asuI GTGG TCCTGC	cac81 scf1 pst1 fnu4HI bsoFI bbvI bsrDI bsg1 s
5601 GGCTTA	5701 GCAGA	5801 TGTTG

# 5901 ATGITGIGCA AAAAAGCGGI IAGCICCTIC GGTCCTCCGA TCGTTGICAG AAGTAAGTIG GCCGCAGIGI IAICACTCAI GGTIAIGGCA GCACTGCAIA IACAACACGI TTITICGCCA AICGAGGAAG CCAGGAGGCI AGCAACAGIC IICAIICAAC CGGCGICACA AIAGIGAGIA CCAAIACCGI CGIGACGIAI

fnu4HI bsoFI bbvI

nlaIII mslI

> eaeI cfrI

acil fnu4HI bsoFI haeIII/palI

sau3AI
mboI/ndeII[dam-]

dpn[[dam+]
mnl1 dpnII[dam-]
sau96I pvuI/bspCI
avaII mcrI

bsiEI

asuI

aluI

acil

MCFL	bsiEI	bcgI	fnu4HI	bsoFI	acil
					ddel
			rsar	bsrI scal	maeIII hphI csp6I
					sfanī
				<u>ب</u> د	1

TAAGAGAATG ACAGTACGGT AGGCATTCTA CGAAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG 6001 ATTCTCTTAC TGTCATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGAC CGAGTTGCTC

nlaIII

sau3AI	mbol/ndeII[dam-]	dpnI[dam+]	dpnII[dam-]	bstYI/xhoII	alwI[dam-]	AAAACT CTCAAGGATC
		maeII	psp14061	Iumx	asp700 mbolI	MINISTREE MENNISHER AMANDARIE GEGEARAGE AGAACTTTAA AAGTGCTCAT CATTGGAAAA CGTTCTTCGG GGCGAAAACT CTCAAGGATC
	hgiAI/aspHI	bsp1286	tru9I bsiHKAI	mseI bmyI	ahaIII/draI	AGAACTTTAA AAGTGCTCAT CA
hinPI	nnal/crol thaI	fnuDII/mvnI	bstul	bsh1236I	acil	7 0044404000 00004444
ngal hinll/acyl ahall/bsaHI	mspI hpaII	SCIPI	ncil	dsav	Caull hincll/hindll	はなっただけである。

6101 TIGCCCGGCG TCAACACGGG ATAATACCGC GCCACATAGC AGAACIIIAA AACAGGCCGC TCAAGAAGCC CCGCTTTTGA GAGTTCCTAG

hphI mbol/ndell[dam-] sau3AI sfaNI mboll[dam-] eco57I dpnI[dam+] alw44I/snoI hgiAI/aspHI apaLI/snoI bsp1286 **DSIHKAI** bmyI mbol/ndeIl[dam-] tagI dpnII[dam-] alwI[dam-] dpnI[dam+] bsrI sau3AI nspBII

6201 TTACCGCTGT TGAGATCCAG TTCGATGTAA CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAG AATGGCGACA ACTCTAGGTC AAGCTACATT GGGTGAGCAC GTGGGTTGAC TAGAAGTCGT AGAAAATGAA AGTGGTCGCA AAGACCCACT CGTTTTTGTC bssSI maeIII bstYI/xhoII aciI

dpnII[dam-]

hphī

Idss ear1/ksp6321 IIoqu mslI fnu4HI aciI **bsoFI** 

TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA ATACTCATAC TCTTCCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA CTTCCGTTTT ACGGCGTTTT TTCCCTTAIT CCCGCTGTGC CTTTACAACT TATGAGTATG AGAAGGAAAA AGTTATAATA ACTTCGTAAA TAGTCCCAAT 6301 GAAGGCAAAA

hinPI

fnuDII/mvnI bstul

**bsh1236**I acil

nlaIII rcal

maeII hinll/acyI

6401 TIGICICAIG AGCGGATACA TAITIGAAIG TAITIAGAAA AATAAACAAA TAGGGGTICC GCGCACAITI CCCCGAAAAG IGCCACCIGA CGICTAAGAA AACAGAGIAC ICGCCITIIC AIAAAITIIT ITAITIGIII AICCCCAAGG CGCGIGIAAA GGGGCTITIC ACGGIGGACI GCAGAIICII ahali/bsaHi aatii ddei nlaIV hhaI/cfoI bspHI acil bsmAI bsrBI

sau96I

IIoqu haeIII/palI asuI

bpuAI Isqq eco01091/draII mplI bssSI

tru9I

rcal

IHdsq

nlaIII

mseI

6501 ACCATTATTA TCATGACATT AACCTATAAA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCGG GAAAGCAGAA GTT

FIG. 41U

>length: 6563

```
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266 4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897 5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
                                                                                                                                                                                                                                                                                                                                                                                                                                  2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
                                                                                                                            2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                                                                                                                                                                                                                                                                                                                                                                                                             72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                                                                                                    178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
                                                                                                                                                                                                                                                                                                                            1645 1813 2616 2637 2751 3408 6107 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                905 930 4234 6166
                                                                                                                                                                                                                                                                                                                                                         5435 5454 6146
                                                  1093 1963 4449
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    1117 1385 5089
                                                                                                                                                                                                                                                                                                                                                                                        ahdI/eam11051(GACNNNNNGTC): 346 5566
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   see tth1111
                                                                               3867[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1 391 4093
                                                                                                                                                                                                                                                                           1307 4678
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         6196 6214
                                                                                                                                                                                                                                              see hinlI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            see hgiAI
1645 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           see aseI
                             403 823
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         5922
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             5742
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 1695
                                                                                                                                                                                                                                                                                                    1788
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        alwni[dcm-](CAGNNNCTG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               aseI/asnI/vspI(ATTAAT):
                                                                                                                                                                                                                                                                                                                                   ahaII/bsaHI(GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      alw441/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                              ahaIII/draI(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            apaLI/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  asp700(GAANNNTTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  apyI[dcm+](CCWGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 alwI[dam-](GGATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               asp718(GGTACC):
                           acc651 (GGTACC):
                                                                                   accIII(TCCGGA):
                                                                                                                                                                                                                                                                                 aflii(ACRYGT):
aatII(GACGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           apol(RAATTY):
                                                        accI(GTMKAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   apal(GGGCCC):
                                                                                                                                                                                                                                                                                                            ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                asul(GGNCC):
                                                                                                                                                                                                                                                                                                                                                                                                                     aluI (AGCI):
                                                                                                                acil(CCGC):
```

#### FIG. 41V

Stop Template Primer

5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' SL.97.2

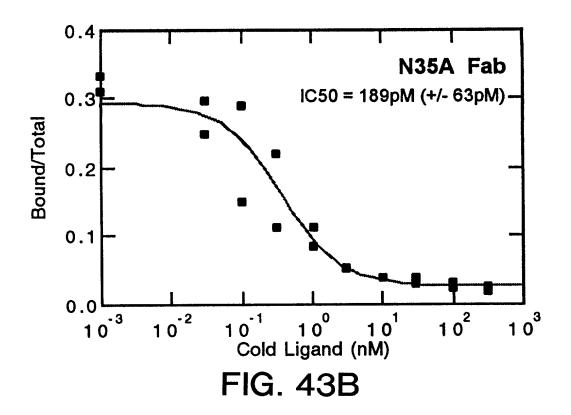
5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' NNS Randomization Primer SL.97.3

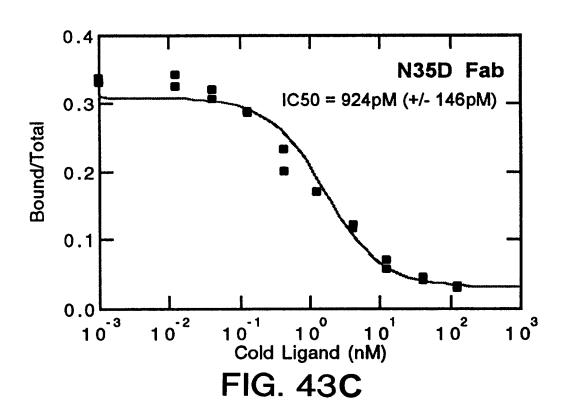
FIG. 42

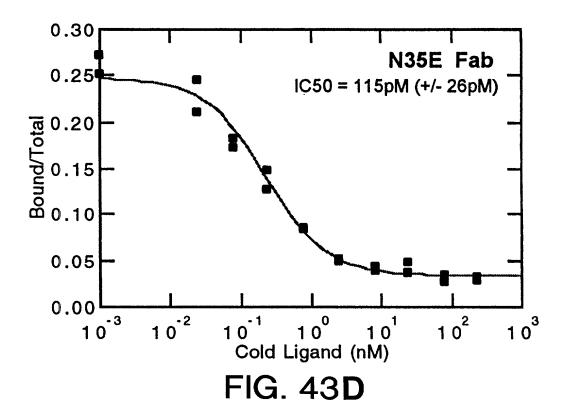
Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

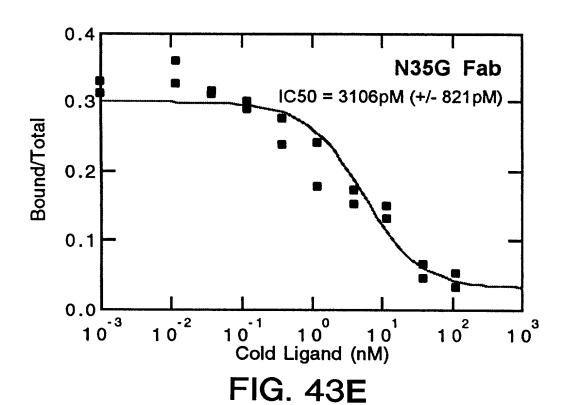
Phage Display (NNS Codon Library) Sort #3	ty (NNS Co	don Libra	ry) Sort #3
Amino Acid	Frequency % Total	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	9	16.6	3.1
Aspartic Acid	8	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine		5.6	N
Serine	<del></del>	1.9	QN N

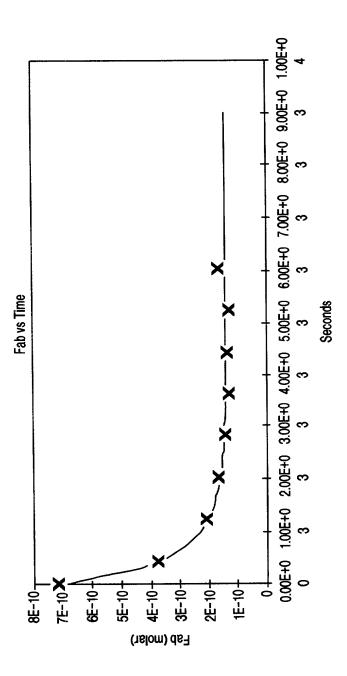
FIG. 43A











Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')2.

kd Kd	ND 114pM	2.1x10 <sup>-4</sup> 109pM	2.6x10 <sup>-4</sup> 54pM
ka	Ð	$2.0x10^6$	4.7x10 <sup>6</sup>
SAMPLE	6G4V11N35A-Fab	6G4V11N35A-F(ab') <sub>2</sub>	6G4V11N35E-Fab

FIG. 44

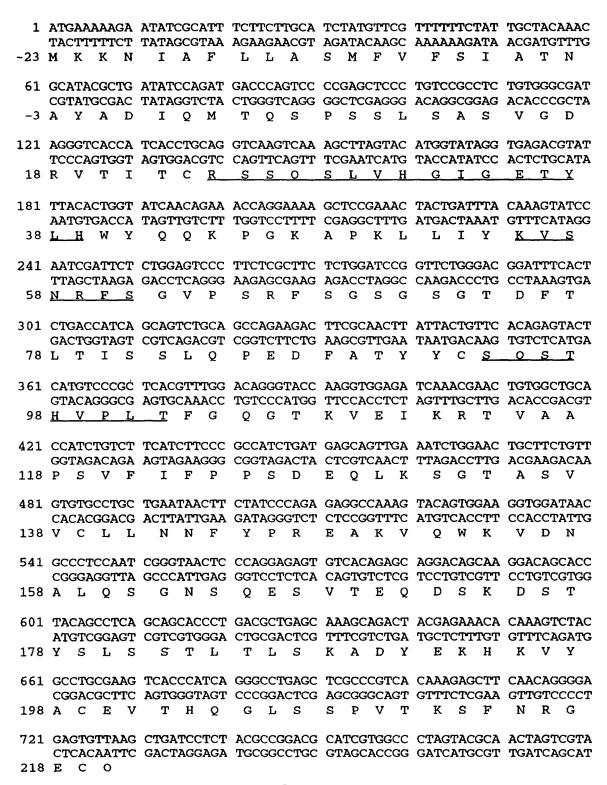
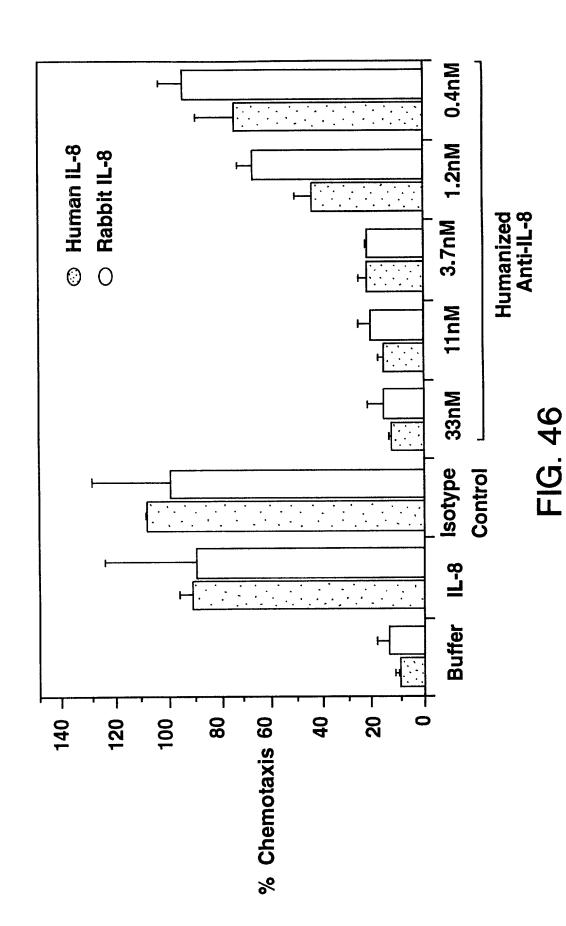


FIG. 45



N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGGTCCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTC-3'

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT AG-3'

Bold indicates nucleotide change destroying Pvull site.

FIG. 47

```
>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)
                                                                                                                                             >made from pSVI.WTSD.D by adding a linearization linker(LL) into the Hpal site
                       > /home/ruby/vc/Immbio/afan/ss.p6G425v11.N35A.choSD
> Wed May 7 18:27:36 1997
                                                                                             > length: 8120 (circular)
                                                                   > sites: std
```

apyI[dcm+] nlaIV ecoRII SCIFI bstNI dsaV mvaI bsaJI bsmFI mbol/ndell[dam-] nspBII pvuli sau3AI aluI hinfI taqI[dam-] pvul/bspCI
pleI dpnII[dam-] dpnI[dam+] taqI[dam-] bsiEI MCLI rmaI bfaI maeI hgiAI/aspHI ecl136II cac8I bsp1286 bsiHKAI hgiJII aluI banII sstI bmyI sacI

1 ITCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC CCAGGCAGCA AAGCTCGA GACTCTCAG GGGTCCGAGG GGTCCGAGG GGTCCGTCGT AAGCTCAG GGGTCCGAGG GGTCCGAGG GGTCCGTCGT AAGCTCAG GGGTCCGAGG GGTCCGTCCGT

Laria	TOTNÅÅ	iibii/avaiii	nlalli	Tuds	nspl	IHdsu	cac8I	HOLE COLECTE SHARWARDAD CORPORATION MOVERNOON CONTRACTOR AND CONTR
							cac8I	じじんじじんと
scrFI	1	ecoRII		H	apyI[dcm+]	bsaJI	FI nlaIV	יייייייייייייייייייייייייייייייייייייי
	mval		dsaV				psm	
	SCLFI	mvaI	ecoRII	dsaV	bstNI	apyI[dcm+]	sexAI	
sfani	ppul0I	nsil/avallI	nlaili	Rphī		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1000

101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCG CCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA CTTCATAACT TTCGTACGTA GAGTTAATCA GTCTTGATAC GTTTCGTACG TAGAGTTAAT

nlaIII

styI

201 GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCCAGTTC CGCCCCATTCT CCGCCCCATG GCTGACTAAT TTTTTTATT CAGTCGTTGG GGGTTGAGG CGGGTTGAGG GCGGGTTAGG GCGGGGTAGG GCGGGGTAC CGACTGATTA AAAAAAATAA acil bsaJI ncol bslI dsaI acil bsrI acil acil acil fokl aciI

### FIG. 48A

haeIII/palI mcrI eagl/xmaIII/eclXI eaeI cfrI bsiEI mspI hpaII GCTTATCGG	nlaIII CATGT ACTACCA	rsal csp61 scal CAAGTACTTC GTTCATGAAG
hacrimal morimari marimael eagimael eaeibfai ofrinhel bsliabl	fnu4HI bsoFI bbvI nspBII aciI ATCCCGCTG CCATCATGGT TAGGGGCGAC GGTAGTACCA	xmnI asp700 GGAACGAGTT
rmaI maeI styI bsaJI bluI avrII[dam-] haeIII/palI anlI stuI mnlI haeI bseRI mnlI bfaI rCTTCATCAT TTTGGAGGC TAGGCTTTTG	mnli TAGAGCGATA AGAGGATTT ATCTCGCTAT TCTCCTAAAA	haell/pall hael scrFl mval bsrBl ecoRll dsaV bstNl acil l apyl[dcm+] bsaJl mnll ddel ccTACCCTGG CCTCCGCTCA
mnll mnll bseRI : AGAAGTAGTG AGGAGGCTTT	maeII maeIII AGTGACGTAA TCACTGCATT	hael hael scrFI scrFI mval_ ecoRII daav bsmAl apyI[d bsal] bsal bsall cccTAACCGT TCTTGCCTCT cccTAACGGACC
fnu4HI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI mnli mnli ddel mnli bsoJi acii haeIII/pali mnli bsoJi acii haeIII/pali mnli bsoJi acii haeIII/pali mnli bsoGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	tfil hinfl acil thal thal fuuDII/mvnI bstUI bsh12361 scarrggaa cgcggarrcc ccgrgccaag	hael scrFI scrFI mval coorli dal bsmAl apyI[dav bslI bsmI bsmNi bshI]  taqI sfaNI bsmFI bsmI apyI[dav bshI]  taqI sfaNI bsmFI bsmI apyI[dav bshI]  taqI sfaNI bsmFI bsmI apyI[dav bshI]  bsaI bsaII bsaII bsaII bsaII bsaII  bsaI cccTGG ccTGCCGGGCCCGGGCCCCGGGCCCCGGGCCCCGGCCCCCGGCCCC
hael: mnl1 bi 301 TATGCAGAGG CO	scrFI nciI mspI hpalI dsav caulI 401 CCGGGAACGG TGCATTGGAA GGCCCTTGCC ACGTAACCTT	taqI 501 TCGACCATTG AA AGCTGGTAAC T

## FIG. 48B

scrFI mval ecoRII dsaV bstNI hinfI mseI sexAI ddeI mboII taqI ahaIII/draI	saci hgiJii hgiJii hgiJiiiiiiiiiiiiiiiiiiii	haell/pall hael scrFl mval ecoRll dsaV tfil dsaV bstNl nlaIII bstNl ddel plel apyl[dcm+] hinfl apyl[dcm+] hinfl sACAAAT GGCCTTCGG TACTTAGTTG GTCCGGTGGA ATCTGAGAAA
eco571  eco571  mbol1  earl/ksp6321  mili  mnli  entl/ksp6321  mnli  entl/ksp6321  hinfI hphI apyl[dcm+] ddel mbol1 taq1 ahall  sexi  fill alwn![dcm-]  sexi  ecoRii  dal  hinfI hphI  sexi  sexi  ecoRii  dal  hinfI apyl  sexi  ecoRii  apyl[dcm+] ddel mbol1 taq1 ahall  sexi  fill msel  sexi  sexi  ecoRicottc TCAGGGGAA GGTAAACAGA ATCGGGGAAATTAAA  fill msel  sexi  sexi  ecoFil  apyl  ddel mbol1 taq1 ahall  sexi  fill msel  sexi  sexi  cancrificat alaccarca alaccarca agacarata agacacarca agacacara agacacarca agacacara agacacarca agacacara	ssti saci hgiJII hgiAI/aspHI ecl136II bsp1286 bsiHKAI bmyI mnll aluI msel ddel bssSI banII bssSI banII bstXI fokI sfaNI msel 701 AGGACAGAAT TAATATAGA AACTCAAAGA ACCACCACGA GGAGCTCATT TTCTTGCCAA AAGTTTGAT GATGCCTTAA GACTTATTGA TCCTGTCTTA ATTATATCAA GAGTCATCT TGGTGGTGCT CTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT	mspi hpali bsawi 801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTTTGGATA GTCGGAGGCA GTTCTGTTTA 1GTTGGCCTT AACCGTTCAT TTCATCTGTA CCAAACCTAT CAGCCTCCGT CAAGACAAAT

# FIG. 48C

hinl1/acy1

hgaI

ecoRII SCLFI

mvaI

sau96I avalI asuI

dsaV ecoRI bstNI taqI apoI apyI[dcm+] mnlI clai/bspl06 bsll bsaJI bsaJI pspDI[dam-] cagGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCTAT CGATTGAATT GTCCACAGGT GAGGGTCCAG GTTGACGTGG AGCCAAGATA GCTAACTTAA seq from pRK6G425VH: Cla-AvrII^	scrFI mval fnu4HI ecoRII dsav rmal bstNl bsoFI mael apyl[dcm+] bfaI acil haell/palI GCTAGTGCAG TCTGGCGGT GCTTGTCAGT CGATCACGTC AGACCGCCACCACT L V Q S G G L V Q	scrFI  ncii mspi hpall dsav cauli xmal/pspAl smal smal scrFI ncii scrFI ncii dsav cauli mval bsli ecoRII bsli bsli bsaJI bsli nlalv nlalv nlalv avai haelli/pall nlalv ccol091/drali asuj caccTCAGG CCCGGGTAA GGCCTGGAA CAGGCAGTC GGGCCCATT CCGGACCTT v R Q A P G K G L E
dsav bstNI apyl[dcm+] bsayl TCCCAGGTC CAAGGGTCCAG GT	rn me b b alul CAGAAGTICA GCI STCTTCAAGT CGI	sau96I avaII as nla bsrI TATGCACTGG ATACGTGACT
	rmal rsal mael bpml/gsul[dom-] bfal bsrl csp6l alul AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TTGACGTTGA GTCTTCAAGT CGATCACGTC	pler hinfl taq1 xhol paeR71 paeR71 avai maeIII avai maeIII xGGGGAGGGTCACTA ATGAGGAGG GCTCAGTGAT x
maeIII hphi scfi foki GGTGACACTA TAGATAACAT CCACTTTGCC TTTCTCTCCA CCACTGTGAT ATCTATTGTA GGTGAAACGG AAAGAGAGT	rmaI maeI bfaI TTCTAGTAGC	hgiJII bsp1286 bmyI scrFI mval banII ecoRII dsav bstNI bstNI bsaJI apyI{dcm+} GCCAGGGGGC TCACTCCGTT TGTCCTGTGC AGTTCTGGC GGGTCCCCG AGTGAGGCAA ACAGGACACG TCGAAGACCG p G S L R L S C A A S G
maeIII hphi scfi 1201 ATACGATTTA GGTGACACTA TAGATAI TATGCTAAAT CCACTGTGAT ATCTAT	nlalli styl pflMI ncol dsal bsll fokl 1301 CCACCATGGG ATGGTCATGT GGTGGTACCC TACCAGTAGAAA 1	hgiJII bsp1286 bmyI scrFI mvaI banII ecoRII dsaV bstNI bsaJI apyI[dcm+] 1401 GCCAGGGGC TCACTCCGTT CGGTCCCCG AGTGAGGCAA

tha! fnuDII/mvnI bstUI bsh1236I nruI ATCTCGCGA CAACTCCAAA AACACAGCAT ATCTGGCGT GTTGAGGTTT TTGTGTCGTA S R D N S K N T A Y	hinll/acyl ahall/bsaHI bsrl aatll maelll taql hphl mboll maell caarggracy rggrcyrcg acgrcycgg	scrFI mvaI ecoRII dsay bstNI bstNI sau96I haeIII/palI asuI  t bsp1286 bsp1286 bsp1286 acil bsaJI bmyI mnlI bmyI nspBII apyI [dcm+] crcchagagca ccrcrggggg cAcAgcggcc s AggTTCTCGT gGAGCCCC GTGTCGCGG s R S T S G G T A A
maeli haelil/pall sau961 saal bsaal asul asul ACTACGGT ATTATCAAAA GTTCAAGGGC CGTTTCACTT T	hinli/acyl scfi  psti bsti aatli  bsgi cac8i mnli taqi  bspMi maeIII taqi  Actgcagat gacagcctg cgtgctgagg ctattaccgt ctattactgct gcaagaggg attatcccta catggtgag actctgggg  TGGACGTCTCCCC TATTACCCC TATTACCCCT ACTCCCCT ACTCCCT ACTCCCT ACTCCCCT ACTCCCCT ACTCCCCT ACTCCCCT ACTCCCCT ACTCCCT ACTCCCCT ACTCCCT ACTCCCCT ACTCCCCT ACTCCCT ACTCCCCT ACTCCCT ACTCCCT ACTCCCT ACTCCCCT ACTCCCT ACTCCCT ACTCCCT ACTCCCT ACTCCCCCT ACTCCCT ACTCCT ACTCCT ACTCCCT ACTCCCT ACTCCT ACT	Seque   Sequ
bell sau3AI mbol/ndeII[dam-] mbol/ndeII[dam-] dpnI[dam+] alwi[dam-] alwi[dam-] hphi bsaAi asu1 1501 TGGGTTGGAT ATATTGATGC TATAATCAAAA GTTCAAGGG CGTTTCACTT TATCACAA CAACTCCAAA AACACAGCAT ACCAACCTA TATAACTAGG AAGGTTACCA TATTGATTT CAAGTTCCG GCAAAGTGAA AAGAGGGTTT TTGTGTCGTA ACCAACCTA TATAACTAGG AAGGTTACCA TATTAATTTT CAAGTTCCG GCAAAGTGAA AAGAGGGCT GTTGAGGTTT TTGTGTCGTA ACCAACCTA TATAACTAGG AAGGTTACCA TATTAATTTTT CAAGTTCCG GCAAAGTGAA AAGAGGGCT GTTGAGGTTT TTGTGTCGTA ACCAACCTA TATAACTAGG AAGGTTACCA TATTAATTTT CAAGTTCCCG GCAAAGTGAA AAGAGGCCT GTTGAGGTTT TTGTGTCGTA	scfi  psti  bsgi  cac8i mnli  bspMi  cac8i ddel drdi  1601 ACCTGCAGAGAGCTG CGTGCTGAGA ACACTGCCGT CTATTACTGT GCAAGAGGGG ATTATCGCTA TGGACGTTA CTTGTCGAC GCACGACTCC TGTGACGACGA  1601 ACCTGCAGAC GCACGACTCC TGTGACGCGA CGTTCTCCCC TAATAGCGAT  TGGACGTCTA CTTGTCGGAC GCACGACTCC TGTGACGCAT  1601 ACCTGACGACTCC TGTGACGCATA CGTTCTCCCC TAATAGCGAT  161 L Q M N S L R A E D T A V Y Y C A R G D Y R Y	sau961         m           nlaIV         nlaIV         nlaIV         nlaIV         ee           hgiJII         nlaIV         hgiJII         nlaIV         ee           bsp1201         bsp1286         banI         banI         banI           ecoRII         banII         mvaI         basuI         basuII/pal           dsaV         asuI         mboII         ecoRII         basuII/pal           bstNI hph         mnl         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI hpi         mnl         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil           bstNI bstRII         bstNI hpsil         bstNI hpsil         bstNI hpsil         bstNI hpsil </td

## FIG. 48F

hinpi nlaiv nari bsp1286 kasi bsiHKAI mspl hgiCl cac81 hpall haell baori bsori alali/snol dsav ddel hhal/cfol nspBlI alw441/snol cauli GAACTCAGGC GCCTGACCA GCGCCTGCC GCCTGACGC CGCACGATG N S G A L T S G V H T F P A V L Q	tfil hinfi maeli GACCTA CATCTGCAAC GTGAATCACA AGCCCAGCAA CTGGAT GTAGACGTG CACTTAGTGT TCGGGTCGTT	ahdi/eamil05i sau96i avali avali mval avali mval asul ecoRII dsav bsp1286 bsaJI bsmFI bpuAl bmyl alwNI[dcm-] apyl[dcm+] bbsI mnli GTGCCCAGCA CCTGAACTCC TGGGGGGACC GTCAGTCTTC CACGGGTCGT GGACTTGAG ACCCCCTGG CAGTCAGAAG C P A P E L L G G P S V F
maelli hphi mspi hpali cfrl01/bsrFl bsawi agel tth1111/aspl GAACCGGTGA CGGTGTGG CTTGGCCACT GCCACAGCAC	4HI NIAIV hgiCI hgiCI pan I pan I pan I pan I pan I pan I AGCTTGGGCA CCCAV TCGAACCCGT GGGTS I G T Q	naeili nspi Arcttgtgac AAAACTCACA CATGCCCACC TAGAACACTG TTTTGAGTGT GTACGGGTGG S C D K T H T C P P
scrFI mvaI ecoRII ecoNI dsaV bstNI bslI apyI[dcm+] fnu4HI bsoFI bbvI 1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCC GACCCGACG ACCAGTTCCT GATGAAGGGG	fnudHI bsolindhi maelli bsp1286 mael bsolindhi maelli bhri maelli bhri bhri bhri bhri bhri bhri bhri bhr	hgiJII beaJI bap1286 beaJI bmyI bmyI 2001 CACCAAGAAAG TTGAGCCCAA GTGGTTCCAC CTGTTCTTTC AACTCGGGTT

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ppvI
                                                                                                                                                                             bbsI bsu361/mstII/sauI
                                                                                                                                                                                          2101 CTCTTCCCC CAAAACCCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTCACATGC GTGGTGGTGG ACGTGAGCCA CGAAGACCCT GAGGTCAAGT GAGAAGGGGG GITTTGGGTT CCTGTGGGAG TACTAGAGGG CCTGGGGACT CCAGTGTACG CACCACCACC TGCACTCGGT GCTTCTGGGA CTCCAGTTCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  2201 TCAACTGGTA CGTGGACGCC GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT GTGGTCAGGG TCCTCACCGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 CACCAGTCGC AGGAGTGGCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         CCTGCACCÃG GACTGGCTGA ATGGCAAGGA GTÁCAAGTGC AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        GGACGIGGIC CIGACCGACI IACCGIICCI CAIGIICACG IICCAGAGGI IGIIICGGGA GGGICGGGGG IAGCICIIII GGIAGAGGII ICGGIIIICCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                      hgaI mnlI
                                                                                                                                mnlI
                                                                                                                                                             bpuAI eco811
                                                                                                                                               mboli ddel
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  CTGTTTCGGC.GCCCTCCTCG TCATGTTGTC GTGCATGGCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        I E K T
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                                                                                                                                                                                                                                                                                                                                                                                                           rsaI
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                                                                                                                                                                                                                                                                                                                                                                                                                                          rsaI
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                                                                                                                                                                               msli bspHI[dam-] asuI bsu36I/mstII/sauI
                                                                                                       nlaIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             K A L
                                                                                                                                  nspHI
                                                                                                                                                                                                                              ပ
                                                                                                                     Idsu
                                                                                                                                                                                                                                                                                                fnuDII/mvnI
                                                                                                                                                                                                                                                                                                                                                                                                                                                        bseRI
                                                                                                                                                                                                                                                                                                                                                                                                                                          mnlI
                                                                                                                                                                                                                                                                                                                                               sacII/sstII
                                                                                                                                                               eco811 maeIII
                                                                                                                                                    mslI
                                                                                                                                                                                                                                                                                                                               bsh1236I
                                                                                                                                                                                                                                                                                                                                                            nspBII
                                                                                                                                                                                                                                                                    acil
                                                                                                                                                                                                                                                                                                                 bstul
                                                                                                                                                                                                                                                                                                                                                                                                                                          fnu4HI
                                                                                                                                                                                                                                                                                    thaI
                                                                                                                                                                                                                                                                                                                                                                                                            bsaJI
                                                                                                                                                                                                                                                                                                                                                                                kspľ
                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsoFI
                                                                                                                                                                                                                                                                                                                                                                                            dsaI
                                                                                                                                                                                                                                                                                                                                                                                                                           acil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            X V S N
                                                                                                                                                     ddeI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      T
K
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 bsmAI
                                                                                                                    mbol/ndell[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               bsaI
sau96I
             nlaIV
                                                                                                        sau3AI avaII
                                                                                                                                                                   dpnII[dam-]
                                           hpall
                               Idsm
                                                          scrFI
                                                                                                                                                  rcal dpn1[dam+]
                                                                                                                                      caulI
                                                                                         dsav
                                                                          ncil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       AGTIGACCAT GCACCTGCCG CACCTCCACG TATTACGGTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       N A K
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X
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                                                                                                                                      nlaIII
                                                                                                                                                                   mnlI
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K
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E
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                                                                                                                                                                                    bsaJI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       NWYOOG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                ecoNI bstNI bsrI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  bsli apyl[dcm+]
                                                                                                                                                                                                                                                                                                                                                                                                             maell
                                                                                                                                                                                                                                                                                                                                                                                                                                                             bsrI bsaAI
                                                                                                                                                                                     ear1/ksp6321
                                                                                                                                                                                                                                                                                                                                                                                                                                             csp6I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     ecoRII
                                                                                                                                                                                                                                                                                                                                                                                                                               rsaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        SCLFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     dsav
                                                                                                                                                                                                                                  L
F
P
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      mvaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                II
II
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scrFI mval ecoRII dsav bstNI apyl[dcm+] bspMI TGACCTGCCT GGTCAAAGGC TTCTATCCCA ACTGGACGGA CCAGTTTCCG AAGATAGGGT T C L V K G F Y P S	plei hinfi nlaIV mboli scfl cac8I GGACTCCGAC GGCTCCTTCT TCCTCTACAG CCTGAGGCTG CCGAGGAAGA AGGAGATGTC D S D G S F F L Y S	sapi mboli mnli eari/ksp632i crccacaacc actacaccca Gaagagccrc gacgrgrigg rgargrgcgr crrcrcggag L H N H Y T Q K S L
SCIFI   DOI	mspl hpali fnu4Hl bsoFl bbvi GGCAGCCGGA GAACAACTAC AAGACCACGC CTCCCGTGCT CCGTCGCCCT CTTGTTGATG TTCTGGTGC GAGGGCACGA Q P E N N Y K T T P P V L	mboli bpuAl hpulol hphi alui bsal bsoFi xmnl bbsi nsil/avalii slui bsaJi bbvi asp700 nlalii sfaNi mnli carcercac grogacdar graggogaac grotercat gercogrost gercacaca graggogaac grocercat graggost crocercat graggost crocerca
aval bi 2401 CAGCCCGAG AACCACAGT GTCGGGGCTC TTGGTGTCCA 347 Q P R E P Q V	dsal bsli msli bsaJi bsrDi 2501 GCGACATCGC CGTGGAGTGG CGCTGTAGCG GCACCTCACC CTCTCGTTAC 381 D I A V E W E S N G	dsal hphi alui bsaJI 2601 CAAGCTCACC GTGGACAAGA GTTCGAGTGG CACCTGTTCT

#### FIG. 481

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nlalii alwi[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    CTAGCTAGCC CTTAATTAAG CCGCGTCGTG GTACCGGACT TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTTCT TGGTAGACAC
                                                                                                                                                                                                                                                             2801 AATAAAGCAA TAGCATCACA AATTTCACAA ATAAAGCATT TTTTTCACTG CATTCTAGTT GTGGTTTGTC CAAACTCATC AATGTATCTT ATCATGTCTG TTATTTCGTT ATCATAGAA TAGTACAGAC GTAAGATCAA CACCAAACAG GTTTGAGTAG TTACATAGAA TAGTACAGAC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  GATCGATCGG GAATTAATTC GGCGCAGCAC CATGGCCTGA AATAACCTCT GAAAGAGGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCATCTGTG
                                                                                                                                           2701 TCCCTGTCTC CGGGTAAATG AGTGCGACGG CCCTAGAGTC GACCTGCAGA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AGGGACAGAG GCCCATTTAC TCACGCTGC GGGATCTCAG CTGGACGTCT TCGAACCGGC GGTACCGGGT TGAACAAATA ACGTCGAATA TTACCAATGT
                                                                                               fnu4HI
                                                                                                                  bsoFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      ddeI acil
                                                                                                                                 bbvI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       mnlI
               haeIII/palI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      acc65I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       asp718
                                                                                                                                                                                                                                                                                                                                                                                                                                    csp6I
                                                                                                                                                                                                                                                                                                                                                                                                                                                     nlaIV
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     hgici
                                                                                                                                                                                                                                                                                                                                                                                                                       rsaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                    kpnI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      banI
sau96I
                                 asuI
                                                   bsofi nlail
                                                                                                                  aluI haeIII/palI
                                                                                                                                hindili bgli bsaJi
                                                                                                   dsaI
                                                                                  ncol
                                                                   styI
                                 fnu4HI
                 acil
                                                                   Sfil
                                                                                   eaeI
                                                                                                   cfrI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       mnlI
                                                                                                                                                                                                                     rmal
                                                                                                                                                                                                                                  maeI
                                                                                                                                                                                                                                                     bfaI
                                                                                                                                                                                                                                                      psmI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         mplI
                                                                                   mael hincil/hindil
                                                                                                                    bsgI
                                                                                                    pstI
                                                                     scfl
                                                                                                                                    asul bfal acci bspMI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      dsal haelli/pall
                                    taqī
                                                                   rmal sall
                                                                                                    sau96I hinfI
                                                  pleI
                                                                                                                     haeIII/palI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          hhal/cfoI nlaIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                         haeI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          bsaJI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsoFI styI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         ncol
                                                                                                                                                                                                                                                                                                                                                                                                                                                        fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         bbvI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         hinPI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           dpnII[dam-] aseI/asnI/vspI
                                                                                                                                                                                                                                                        sfaNI apol
                                                                                                                                                                                       o
⊭
ʊ
                                                                                                                                                                                                                                                                                                                                       mbol/ndell[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                       taqI[dam-] tru9I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          bspDI[dam-] mseI
                                                                                                                                                                                                                                                                                                                                                                                                                                                         clal/bsp106[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          dpn1[dam+] asp700
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         mbol/ndell[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          XmnI
                                                                                                                                                                                                                                                                                                                                                                        dpnII[dam-]
                                                                     mspI
hpaII
                                                                                                                                         cauli
                                                                                                                                                                                                                                                                                                                                                          dpnI[dam+]
                                        BCIFI
                                                     ncil
                                                                                                         dsaV
                                                                                                                                                                                                                                                                                                                                                                                         pvuI/bspCI
                                                                                                                                                                                      447 S L S P
                                                                                                                                                                                                                                                                                                                           sau3AI.
                                                                                                                          bsmAI
                                                                                                                                                                                                                                                                                                                                                                                                                          bsiEI
                                                                                                                                                                                                                                                                                                                                                                                                          MCLI
                                                                                                                                         bslI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            2901
```

#### FIG. 48J

SCIFI  mvaI  dsav  bstNI  apyl[dcm+]  sexAI  sexAI  TGT GAGGAAAG	acil fokl acctaactec Geecateceg Gegartgag	li ddei I mnli alui mnli haeIII/pali CGGCCTCT GAGCTATTCC AGAAGTAGTG
sfaNI ppul0I nsil/avallI nlalII sphI nsplI nsplI cac8I cac8I cat8I cat8I cat8I cat8I	sfaNI ppul01 nsil/avall1 lall1 nh nspl nspH cac81 CAAAGCATGC ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACGTTTCGTACG TAGAGCATAATTCGTACG TAGACTTAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATACG TAGACCATAATTCGTACG TAGACCATACG TAGACCATACG TAGACCATAATTCGTACG TAGACCATACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACG TAGACCATAATTCGTACATAATTCGTACGTACGTACGACCG GGGATTCGTACGTACGTACGTACGTACGTACGTACGTACG	fnu4HI bsoFI bsoFI bglI sf1I mali mali ddei mali mali mali malui mi mnli bsaJi mili alui m mnli bsaJi acii haeIII/pali bcTGACTAAT TTTTTTTTT TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG
scifi  mval  ppul01  ecoRII  dsaV  bstNI  apy1[dcm+]  bsmJI  bsmJI  cac8I  schid  apy1[dcm+]  bsmJI  cac8I  cac8CacCCCCGGCCCGGCGCGGCGCGGCCCGGCCCGGCC	### scrFI ### ppul01 ####################################	nlaIII styl ncol bsli dsal acil bsaJI ccccccarg GCTGACTAAT TTTTTAT
3001 GAATGTGTGT CAGTTAGGGT CTTACACACA GTCAATCCCCA	nlalv scrfi mval ecoRII eAsA bstNI apyl[dcm+] bsaJI cac8I 3101 rccccAGGCT CCCCAGCAGG CAGAAGTATG AGGGTCCGA GGGGTCGTCC GTCTTCATAC	nlali styl ncol bsl dsal 3201 CGCCCAGTTC CGCCCCATG GCGGGTCAAG GCGGGGTAC

# FIG. 48K

tfir hinfi acii thai fuuDII/mvni bstUI bsh1236I hinfi hA CGCGGATTCC CCGTGCCAAG AGTCAGGTAA IT GCGCCTAAGG GGCACGGTTC TCAGTCCATT	sau3AI mbol/ndeII[dam-] dpnI[dam-] alwI[dam-] taqI[dam-] taqI[dam-] taqI[dam-] bspDI[dam-] sau3AI mbol/ndeII[dam-] dpnII[dam-] dpnII[dam-] AAC CTTTTGGATC GATCTTACTG ACACTGACAT TTG GAAAACCTAG CTAGGATGAC TGTGACTGTA 'TEMOVE ATG 'UZ match lariat consensus' IgG VH natural lariat restored'
scrFI ncil mspi hpall dsav haelil/pall alul mcrI rmal eagl/xmalli/eclXI mael eael bfal cfrI nhel bsiEl cac8I mspi cauli alul hpall alul hpall iTCGAT CGATAGGC GGCCTTGCC ACGTAACCTT iG4VL: AvrII - HindIII frag	fnu4HI bsoFI acil thal thal styl fnuDII/mvnI tru9I bstJI mseI bsaJI bsh1336I aseI/asnI/vspI ccTTGGCTTC GTTAGAACGC GGCTACAATT AATACATAAC GGAACCGAAG CAATCTTGCG CCGATGTTAA TTATGTATTGC 'sp6 promoter
rmal mael styl bsaJI blaI avrII[dam-] haeIII/palI n haeI mnl bfal al and AAACCTCGG ATCCGAAAAG csaAA AAACCTCCGG ATCCGAAAAC csaAA AAACCTCCGG ATCCGAAAAC csaAAAACTTTTC	bstXI sofI sau96I pleI haeIII/pal sofI hinfI asuI cTa TagagrcTaT AggcCCACC icaT atcragaTa
mnli 3301 AGGAGG	acil rsal csp61 3401 GTACCGC

FIG. 48L

avali rmal secret asul scret asul secret maci bfal stand asul styl scret beau clar/bspl06 pflMI styl asul bstNI alui bsvI bstNI bstNI bstNI bstNI alui bstNI bstNI bstNI bstNI alui bstNI bstNI bstNI bstNI cACCATGCG AACCTAGCTT GGCTGCATC GATTGAATTC CACCATGGA AAAAAGAGGT GTCCACAGGGG CTCACAGGGC TTCGATCGAA CCCGACGTAG CTAACTTAAG GTGGTACCTT ^cloning linker	mnli acii ccrgrccgcc rcrgrccgcc ggacagccgc agacacccgc	scrfi mval ecoRII dsaV bstNI aluI apyI[dcm+] GTATCAACAG AAACCAGGAA CATAGTTGTC TTTGGTCCTT Y Q Q K P G K A P K
n. 16 pf. 17 apol 21 apol 21 (dam - ) GATTGAATT	mn acii ccrercece ggacagee	scrFI mvaI ecoRII dsaV bstNI apyI[d AAACCAGGA
seu961  aval1  asul  asul  asul  berFI  mval  cooRII thaI nheI  betNI  betNI  byl[dcm+] mnlI bsh1236I aluI bspl[dam-]  bslI bsaJI nruI aluI bspl[dam-]  bslI bsaJI bsaJI nruI bbvI bspJ[dam-]  tTTTTCTCCA CAGGTGTCCA CTCCAACTGCAC TCGGTTCGCA AAGCTAGCTT GGCTGCATC GATTGAATTC  AAAAAGAGGT GTCCAACTGACGG AAGCTAGCATC GATTGAATTCAACTGAACGC TTCGATCGAACGACGTAC CTAACTTAAG  cloning linker	aluI sstI sacI sacI hqiJII hqiJII hqiJII bsp1286 bsiHKAI bsmFI bmyI bsrI avaI tthllI/aspI banII ATGACCCAGT CCCGAGCTC CCTG	GTATCAACAG CATAGTTGTC Y Q Q
rmal mael bfal hel /mvnl bstUl cac81 bsh12361 aluI rul aluI cGGG AAGCTAGCTT	bsri tth1111/e ATGACCCAGT TACTGGGTCA	maell snaBl bsaAl GGTGCTACGT ATTTACACTG CCACGATGCA TAAATGTGAC G A T Y L H W
maeI thaI nheI fnuDII/mvnI bstUI bsaJI nruI cc TCGGTTCGCG A GG AGCCAAGCGC T	rsal bpml/gsul[dcm-] bsrl csp61 ecoRV  ACTGCAACTG GAGTACATTC AGATATCCAG TGACGTTGAC CTCATGTAAG TCTATAGGTC  D I Q	maell snabl bsaal GGTGCTACGT CCACGATGCA G A T Y
the transfer of the transfer o	rsal bpml/gsul[dcm-] bsrl csp61 ACTGCAACTG GAGTACATTC TGACGTTGAC CTCATGTAAG	AI p6I nlaIII ACATGGTATA TGTACCATAT H G I
sau961 avaII asuI scrFI mvaI ecoRII dsav bstNI apyI[dcm+] crcccAGGTC CA		rsal ddel alul csp6I hindIII nl AAAGCTTAGT ACI TTTCGAATCA TGT
beli caggigicca ( grccacaggi	rmal mael foki bfal TCATCCTTTT TCTAGTAGCA	NI AGGTCAAGTC TCCAGTTCAG R S S Q
TTTTTCTCCA	foki TCATCCTTTT AGTAGGAAAA	scfi psti bsgi hphi sse83871 ddei maeIII bspMI aluI csp6I bstEII hphI bspMI hindIII nlaIII ATAGGGTCAC CATCACCTGC AGGTCAAGTC AAAGCTTAGT ACATGGTATA TATCCCAGTG GTAGTGACA TCCAATACT TTTCCAATCA TGTACCATAT R V T I T C R S Q S L V H G I
CCACTTTTC	nlaIII 3601 TGGTCATGTA ACCAGTACAT	hphi maeili bsteii ATAGGGTCAC TATCCCAGTG
3501	3601	3701

# FIG. 48M

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haeIII/palI
                                                                          fnu4HI
                                                                                       bsoFI
                                                                                                  bbvI
                                                                                                                                                                                                                                                                          mbol/ndell[dam-] fnu4HI
                                                                                                                           pstI
                                                                                                                 scfI
                                                                                                                                          bagi
                                                                                                                                                                                                                                                                                       bsoFI
                                                                                                                                                      bbvI
                                                                                                                                                                                                                                                                                                               3901 CAGCCAGAAG ACTICGCAAC TIAITACTGI TCACAGAGIA CICAIGICCC GCICACGIIT GGACAGGGIA CCAAGGIGGA GAICAAACGA ACTGIGGCIG
                                                                                                                                                                                                                                                                                                                             GICGGICIIC IGAAGCGIIG AAIAAIGACA AGIGICICAI GAGIACAGGG CGAGIGCAAA CCIGICCCAI GGIICCACCI CIAGIIIGCI IGACACCGAC
                                                                                                                                                                                                                                                                                                                                          T V A A
                                                                                                                                                                                                                                                                                                                                                                                                          4001 CACCATCTGT CITCATCTTC CCGCCATCTG ATGAGCAGTT GAAATCTGGA ACTGCTTCTG TTGTGTGCCT GCTGAATAAC TTCTATCCCA GAGAGGCCAA
                                                                                                                                                                                                                                                                                                                                                                                                                       GTGGTAGACA GAAGTAGAAG GGCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGAAGAC AACACACGGA CGACTTATTG AAGATAGGGT CTCTCCGGTT
                                                                                                                                                                                                                                                                                                                                                                                  haeI
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                                                                                                                                                                                                                                                                                                   dpnII[dam-]
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                                                                                                                                            bsmFI
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                                                   mbol/ndell[dam-]
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                                                              dpnI[dam+]
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hpaII
             bslI
                          bsaWI
                                       sau3AI
                                                                                                       nlaIV
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## FIG. 48N

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4201 CTGACGCTGA GCAAAGCCAGA CTACGAGAAA CACAAAGTCT ACGCCTGCGA AGTCACCCAT CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG
                                                                                                             4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCCAGGAGA GTGTCACAGA GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC
                                                                                                                           TCATGTCACC TICCACCIAT TGCGGGAGGT TAGCCCATIG AGGGTCCTCT CACAGTGTCT CGTCCTGTCG TTCCTGTCGT GGATGTCGGA GTCGTCGTGG
                                                                                                                                                                                                                                                                                                                                                                                                                               GICCCGGACT CGAGCGGGCA GIGITICICG AAGIIGICCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   4301 GAGAGTGTTA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAAGCAA TAGCATCACA AATTTCACAA ATAAAGCATT
CTCTCACAAT TCGAACCGGC GGTACCGGGT TGAACAAATA ACGTCGAATA TTACCAATGT TTATTTCGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTAA
                                                                                                                                              SST
                                                               fnu4H1
                                                                              ddeI bsoFI
                                                                                              scfI mull bbvI
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bsiHKAI
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FIG. 480

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dsal haelli/pall
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                                                                                                                                                                                                                             4401 TITITCACTG CATICTAGII GIGGITIGIC CAAACTCAIC AATGIAICII AICAIGICIG GAICGAICGG GAAITAAIIC GGCGCAGCAC CAIGGCCIGA
AAAAAGIGAC GIAAGAICAA CACCAAACAG GIIIGAGIAG IIACAIAGAA IAGIACAGAC CIAGCIAGCC CITAAIIAAG CCGCGICGIG GIACCGGACI
                                                                                                                                                                                                                                                                                                                                                                                                                4501 AATAACCTCT GAAAGAGGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC
                                                                                                                                                                                                                                                                                                                                                                                                                               TTATTGGAGA CITICICCIT GAACCAATCC ATGGAAGACT CCGCCTTICI TGGTCGACAC CITACACACA GTCAATCCCA CACCITICAG GGGTCCGAGG
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                                                                                                                                                                   bbvI
                                                                                                                                                                                 hinPI
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                                                                                                                                                                                                                                                             ^sv40 origin
             mbol/ndell[dam-]
                                                                                                                                      bspDI[dam-] tru9I
                                                                                                                                                      mseI
                                                                                                                      clai/bspl06[dam-]
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                                                                                                                                                                    mbol/ndell[dam-]
                                                                                                                                                                                 dpnI[dam+] xmnI
                                          dpnII[dam-]
                              dpnI[dam+]
                                                           Dasd/Invo
                                                                                                       tagI[dam-]
sau3AI
                                                                                                                                                                                                               nlaIII alwi[dam-]
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### FIG. 48P

4601 CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC GGTCGTCCGT CTTCATACGT TICGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCGTCC GTCTTCATAC GTTTCGTACG

sexAI

IHdsu

Idsu

sphī

cac8I

cac8I

bsmFI nlaIV

bsaJI

apy1[dcm+]

nspHI cac8I

cac8I

sphI nspI

dsaV bstNI

apyI[dcm+]

bstNI

I GCTGACTAAT CGACTGATTA	maeIII alui PAAAAGCTG PTTTTTCGAC	scrFI mvaI ecoRII dsav bstNI apyI[dcm+] bsaJI GGGAAAACCC
nlaII styI ncoI bslI dsaI aciI bsaJI CCGCCCCATG	rmai maei styi bsaji bsaji blui avrii[dam-] haeili/pali stui haei mnli bfai alui mrigagggc TAGGCTTTTG CAAAAAGCTG AAACCTCCGG ATCCGAAAAC start pUC118^	bsrI maeII maeIII TTACAA CGTCGTGACT
acil bsri acil TAACTC CGCCCAGTTC CGC ATTGAG GCGGGTCAAG GCC	mnli mnli bseRI STAGTG AGGAGGCTTT TTT	haeIII/ eael cfrI bsrI CACTGGCCGT
acil bsmFI acil foki GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATTCT CAGTCGTTGG TATCAGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GCGGGTAAGA	4HI I/pall II/pall mnli ddel bsaJI mnli aluI if haeIII/palI GC CTGGGCCTCT GAGCTATTCC AGAAC	ThinpI hinpI hal/cfol hhal/cfol hhal/cfol funDII/mvnI funDII/mvnI hstUl hal/cfol scfl tru9I cac8I tru9I pstI msel tru9I bsh1236I msel bsgHII swal sse8387I atta ATTAAGGCGC GCCATTTAAA TCCTGCAGGT AACAAAAT TAATTCCGCG CGCTAAATTT AGGACGTCCA TTGT inker inserted into Hpal site
acil bsmFl 4701 ATCTCAATTA GTCAGCAACC ATAGTCCCGC TAGAGTTAAT CAGTCGTTGG TATCAGGGCG	fnu4HI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI bsoFI mnlI mnlI ddeI mnlI bsoJI mnlI aluI mnlI bsoJI acii haeIII/palI mnlI bsoJI acii haeIII/palI mnlI bsoJI acii haeIII/palI mnlI bsoCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	fnu4HI haeIII/palI hinPI mcrI hhal/cfoI eagl/xmaIII/eclXI thal eaeI hubDII/mvnI eaeI bsrUI bstUI bsrBI bsoFI hinPI taqI cfrI hhal/cfoI scfI xhoI fnu4HI tru9I cac8I tru9I pstI paeR7I bsiEI pacI ascI ahaIII/draI avaI bsoFI mseI tru9I bsh1236I mseI bsgI maeIII mlI aciI aciI aciI mseI bssH136I mseI sse8387I aluI 4901 TTACCTCGAG CGCCCTTA ATTAAGGCG CGCATTTAAA TCCTGCAGGT AACAGCTTGA AATGGAGCTC GCCGCAAT TAATTCCGC CGGTAAATTT AGGACGTCCA TTGTCGAACC ^1inearization linker inserted into Hpal site

# FIG. 48Q

sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] vvul/bspCI iorI siEI GGTC GCCTTCCCA ACAGTTGCGT	hinPI thai thai fuuDII/mvni bstUI scfI bsh1236I rsaI hhai/cfoI csp6I bslI cAACCATAGT ACGCGCCTG GTTGGTATCA TGCGCGGGAC	mboli ctttcgcttt cttcccttcc gaaagcgaaa gaagggaagg
sau961 haeIII/palI asuI mulI aciI p mboII cac8I m earI/ksp6321 b CGAAGAGGCC CGCACC	acil maell TCACACCGCA TACGICAAAG AGTGTGGCGT ATGCAGTFTC	hinpi hhal/cfol rmal hinpi haeli hhal/cfol bsrBi hhal/cfol bsrBi haeli mael acil cac8i bfal cac8i cTACACTTGC CAGGGCCCTA GGGGCGGGGGGGGAG
cac8I aluI pvuII nspBII fokI cac8I ACATCCCCC TTCGCCAGCT GGCGTAATAG	sfani acii TATTTTCTCC TTACGCATCT GTGCGGTATT ATAAAAGAGG AATGCGTAGA	fnu4HI bsoFI hinPI hinPI hhal/cfoI thal thal fnuDII/mvII bstUI bstUI bstUI maeIII bbvI maeIII GGTTACGCGC AGCGTGACCG CTACACTTGC CAGCGCCCTC CCAATGCGC TCGCACTGC GATGTGAACG GTCGCGCGCGGGGGGGGGG
fnu4HI tru9I bsoFI maeIII mseI bbvI 5001 TGGCGTTACC CAACTTAATC GCCTTGCAGC A ACCGCAATGG GTTGAATTAG CGGAACGTCG T	hinPI hhal/cfoI hhal/cfoI nlaIV narI kasI hinli/acyI hgiCI haelI aciI banI sfaNI	nI SGTGTGGT CCACCA

nlaIV hgici taqi bani mnli FA GTGCTTTACG GCACCTCGAC	maell plei tru91 plei drdi hinfi maeli msei hinfi TGACGTTGGA GTCCACGTTC TTTAATAGTG GACTCTTGTT ACTGCAACCT CAGGTGCAAG AAATTATCAC CTGAGAACAA	tru91 msel haeIII/pall alul msel AAGGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTTAA TTCCCTAAAA CGGCTAAAGC CGGATAACCA ATTTTTACT CGACTAAATT	acil fnu4HI bsoFI tru9I sfaNI mseI acil CT GCTCTGATGC CGCATAGTT& AGCCAACTCC GA CGAGACTACG GCGTATCAAT TCGGTTGAGG	SfaNI   SfaNI   IL/dfol   mspl   hpall   hpall   scrFI     hpall   scrFI     hoil   dsav fokl   drdl   daul   adil   ddl   d
nlalv hgiJii bsp1286 bmyi nlalv ATCGGGGCT CCCTTTAGGG TTCCGATTTA TAGCCCCCGA GGGAAATCCC AAGGCTAAAT	maell p drdl ATAGACGGTT TTTCGCCCTT TGACGTTGG TATCTGCCAA AAAGCGGGAA ACTGCAACC	TTTGATTTAT AAGGGATTTT GCCGATTTC AAACTAAATA TTCCCTAAAA CGGCTAAAG	hgiAI/aspHI bsp1286 bsiHKAI bmyI ddeI apaLI/snoI rsaI alw44I/snoI csp6I CAATTTTATG GTGCACTCTC AGTACAATCT	hinPI hhal/cfol thal thal funDII/mvnI bstUl bstUl acil acil hgal drdi ccGCCAACAC CCGCTGACGC GGCGGTTGTG GCGGACTGCC
mspl hpall nael cfrl01/bsrFl maell cac8l 5301 TTCTCGCCA CGTTCGCCG CTTCCCCGT CAGGTCTAA AAAGAGGGGT GCAAGCGGCC GAAAGGGGCA GTTCGAGATT 7	maeII haeIII/palI draIII sau96I hphI bsaAI asuI 5401 TTGATTTGGG TGATGGTTCA CGTAGTGGGC CATCGCCCTG ATAGACGGTT TTTCGCCCTT	tru9I bsli aval bsli aval 5501 CCAAACTGGA ACACACTC GGGCTATTCT TTGATTTAT AAGGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTTAA GGTTTGACCT TGTTGTGGT TGGGTAAGA AAACTAAATA TTCCCTAAAA CGGCTAAAGC CGGATAACCA ATTTTTTACT CGACTAAATT	thal fnuDII/mvnl maeII tru9I apol tru9I psp1406I msel bstUI msel tru9I apol bsh1236I sspl msel 5601 CAAAAATTTA ACGCGAATTT TAACAAAAT TGACGTAAA ATTGTTTAT AATGCAAAT	hinPI fnu4HI maeIII bsoFI maeII bsrI nlaII hhaI/cfoI bsaAI tth1111/aspI bbvI 5701 GCTATCGCTA CGTGACTGG TCATGGCTGC GCCCCGACAC CGATAGCGAT GCACTGACCC AGTACCGACG CGGGGCTGTG

pall I rall TGA ACT	ATT TAA	I TTC AAG	hgiAl/aspHI bsp1286 bsiHKAI dam-] bmyI apaLl/snoI alw441/snoI cGC
mnli haeIII/palI sau96i asuI bsSI eco1091/draII AG GGCTCGTGA	TTTGTTTATT AAACAAATAA	msli TCAACATTTC AGTTGTAAAG	hgial bspl2 sau3AI bspl2 sau3AI bsiHX mboI/ndeII[dam-] dpnI[dam+] bmyI dpnI[dam+] bmyI eco57I apail sfaNI mboII[dam-] alw44 AAGTAAAAGA TGCTGAAGAT CAGTTGGGTG TTCATTTTCT ACGACTTCTA GTCAACCCAC
nI mbolI ss bpuAl eco bbsI eco AGTATTCTTG AAGACGAAAG TCATAAGAAC TTCTTC	nlaIV acil thaI thaI fnuDII/mvnI bstUI bstUI hinPI hhaI/cfoI AAATGTGGGC CGTTGGGGAT	mboli eari/ksp6321 AAAAGGAAGA GTATGAGTAT TTTTCCTTCT CATACTCATA	sau3AI mboI/nde dpnI[dam dpnII[da eco571 mboII[dam-] crcaAGAT CAGT
mboli bpual basi rrctig aagi	acii thai thai fuuDii/m bstUi bsh1236i hinPi hhai/cfoi srGCGC GGAA	mboli earl/ksp6321 sgaaga gtatga ccttct catact	sfani Saaaa Tittot acc
mvbl	G AAATC	A AAAAC	i SA AAGTU
thal fnuDII/mvnI bstUI bsh12361 hinPI hhal/cfoI thal mnlI fnuDII/mvnI bstUI bsh12361 bsh12361 cGCGCGAGGC AGTATTCTTG AAGACGAAAG GGCCTCGTGA GCGCGCACCT GCGCACCTCCTCTTC AAGACGAAAG GGCCTCGTGA	CTTTTCGGG	mboli sspi eari/ksp6321 ataatattga aaaaggaaga gtatgagtat tattataact ttttccttct catactcata	hphI ACGCTGGTGA TGCGACCACT
hphI ATCACCGAAA TAGTGGCTTT	acyl beahl :CAGGTGGCA	AAATGCTTCA TTTACGAAGT	hphi rttttgc tcacccagaa aaaaacg agtgggtctt
hphI TTTCACCGTC 7	nlaIV  acii thai thai fuuDII/acyi bstui bstui ahaii/bsaHi bsh1236i aatii hinPi hinPi ddel maeli hhai/cfoi TTCTTAGACG TCAGGTGGCA CTTTTCGGG AAATGTGCGC GGAACCCCTA TTTGTTTATT AAGAATCTGC AGTCCACCGT GAAAAGCCC TTTACACGC CCTTGGGGAT AAACAAATAA	TAACCTGAT AAATGCTTCA ATTGGGACTA TTTACGAAGT	hphi ctgtttttgc tcaccagaa gacaaaaacg agtgggtctt FIG. 48T
scrFI ncil mspi hpali nspi dsav nspHi esp3i fnu4Hi bsmBi bbvI .I bsmAi bbvI bsl cauli alui nlaili mnll hphi ccgtctccg gactgcatg tctcacaca aactgcatg	TAATAATGGT 7	rcal bspHI bsrBI bsmAI acii nlaIII TGTATCCGCT CATGAGACAA TAACCCTGAT	TTTGCCTTC (
nspI   nspH   fnu4HI   bsoFI   bbvI   mnlI   caluI nlaiII   mnlI   crcacacgt   crcacacgt	nlaiii tru9I rcai msei bspHi TTTATAGGTT AATGTCATGA	rcal bspHI bsrBI bsmAI acil nlaIII CATTCAAATA TGTATCCGCT CATGAGACAA GTAAGTTTAT ACATAGGCGA GTACTCTGTT	fnu4HI bsofI acil TTATTCCCTT TTTGCGGCA TTTTGCCTTC AATAAGGGAA AAAACGCCGT AAAACGGAAG
		CATTCAAATA GTAAGTTTAT	fnu4HI bscipscorr fnu4HI bscript corrected analoggang ground grou
aluI GAAGCT GITCGA		6001 TTTCTAAATA AAAGATTTAT	CGTGTCGCCC
5801	5901	6001	6101

AspHI 86 tru9I AI mseI ahaIII/draI CTT TTAAAGTTCT SAA AATTTCAAGA	rsal csp61 bsr1 scal hph1 maeIII AGTA CTCACCAGTC	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] pvul/bspCI mcrI bsiEI CTGACAACGA
hgiAI/aspHI bsp1286 tru9I bsiHKAI mseI bmyI ahaIII/ s ATGAGCACTT TTAAA	rsal csp61 scal h r TGGTTGAGTA CT	haeIII/palI aeI frI u4HI oFI iI GGC CAACTȚACTT
maell psp14061 xmn1 asp700 oll AGACG TTTTCCAAT	ddel trct cagaatgac	hael eael cfrl fnu4HI bsoFI acil acil sATA ACACTGCGGC
P. xm. xm. as: as: mboli TCGCC CCGAAGA.	acil inu4HI soFI SCCGAT ACACTAT	fnu4HI bsoFI bbvI mslI nlaIII GC TGCCATAACC ATGAGT
sau3Al nspBII sau3Al maeII mbol/ndeII[dam-] mbol/ndeII[dam-] mbol/ndeII[dam-] dpnI[dam+] mbol/ndeII[dam+] mbol/ofol bstYl/xhoII dpnII[dam-] alwI[dam-] alwI[dam-] mbolI mbolI mbolI maeIII taqI alwI[dam-] aciI bstYl/xhoII mbolI mboII maeIII taqI alwI[dam-] aciI bstYl/xhoII mboII mboII maeIII taqI alwI[dam-] aciI cacaacacacacacacacacacacacacacacacacac	acil ncil thal thal fuuDII/mvnI hpalI bstUI bstUI bsh1236I hinli/acyl mcif fnu4HI hinPI hall/cfol ahall/bsaHI bcgl bsiEl bsoFi cGATACCG GGCATAATAT CCGTGATGT GGGCCGTT CTGTTGAGCA GTCTTACTGA ACCACAGG GCGTCAGGCCGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCAGG	TATGCAGT
sau3AI nspBII mbol/ndell[dam-] dpnl[dam+] stYl/xholi dpnl[[dam-] lw[[dam-] cGATCTCA ACAGCGGTAI	scrFI ncil mspi hpali dsav hinll/acyl hgal cauli ahall/bsaHI cA CGCCGGCAA	I CA GTAAGAGAA: GT CATTCTTT
sau3AI ns mbol/ndell  dpnI[dam+] bstYl/xhoII bsrI dpnII[dam-] I alwI[dam-] AA CTGGATCTCA ACJ	I  }  AT CCGTGATC  TA GGGCACTAC	foki nlaiii GGA TGGCATGAC CCT ACCGTACTG
E maeIII taqI TGGG TTACATCGAP ACCC AATGTAGCTT	acil thai fnuDil/mvnI bstUI bsh12361 hinPI hal/cfoI rrGGC GGGGTATTA	sfani foki nlaiii ACAGAAAAGC ATCTTACGGA TGGCATGACA GTAAGAGAAT TGTCTTTTCG TAGAATGCCT ACCGTACTGT CATTCTCTTA
bssSI 6201 CACGAG GTGCTC	6301 GCTATG	6401 ACAGAA

#### FIG. 481

mbol/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
nlaIII alwI[dam-]

sau96I avaII

sau3AI maeIII nlaIII

mspI sau3AI nlaIV mbot~~~

it 'asni/vspi ATA	AI			sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] GA
truS msel aselv ACAATTAA	/bsrFI bsmAI I bsaI m-] bsaI GAGCGTGGGT CTCGCACCCA	AACGAAATAG TTGCTTTATC	tru9I msel ahaIII/draI msel ATTTAAAACT TCATTTTTAA	GTAGAAAA
mspI hpall aluI scrFI aluI nciI el dsaV ial caulI AG CTTCCCGCCA	mspI hpall cfr101/bsrFI nlaIV hphI bpmI/gsul[dcm-] bsa. CTGATAAATC TGGAGCCGGT GACCGTGGGT	foki A ACTATGGATG F TGATACCTAC		hgaI .Gc GTCAGACCCC
rm ma bi CTTACTCI GAATGAGA	E CTGATAAATC CGACTATTTAG	pleI hinfI ahdI/eam1105I ACACGACGG GAGTCAGGCA TGTGCTGCCC CTCAGTCCGT	CTTTACATTG	maeli tru9i msel cccTTAACGT GAGTTTTCGT TCCACTGAGC GGGAATTGCA CTCAAAAGCA AGGTGACTCG
bsrI 191 I.I. AC TGGCGAACTA TG ACGCTTGAT	C TGGTTTATTG G ACCAAATAAC		A CTCATATATA T GAGTATATA	II T GAGTTTTCGI
hinp! hhal/cfo! mst! avill/fspl bs; I mse! fi TGCGCA AACTATTAAC	bgll cac81 haelII/pall asul mspl ol hpall GGCCCT TCCGGCACCG	TC GTAGTTATCT AG CATCAATAGA	AG ACCAAGITIA	maeII tru9I mseI AT CCCTTAACGT IA GGGAATTGCA
hinpl hhal/ mstl avill/ maell psp14061 ACA ACGTTGCGCA	PI I/cf GCTC CGAG	pali mnli ATGGTAAGCC CTCCCGTATC TACCATTCGG GAGGGCATAG	maeIII GCATTGG TAACTGTCAG	nlaiii rcai bsphi PATCTCA TGACCAAAAT TTAGAGT ACTGGTTTTA
hhal/cfol hhal/cfol hhal/cfol bsofl	sau96I avaII hin asuI hha AGTTGCAGGA CCACTTCTGC TCAACGTCCT GGTGAAGACG	haeIII/palI au96I aIV mr GGCCAG ATGGTAAGCC	tru9I mnli msei maeIII cctcactgat taagcattgg taactgtcag accaagttta ctcatatata cttttagattg	rmal mael sau3Al mael sau3Al sau3Al hphl mbol/ndeII[dam-] mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] tru9I bstYI/xhoII alwI[dam-] rcal msel alwI[dam-] bstYI/xhoII bstMI/draI bfaI mboII[dam-] TTTAAAAGGA TCTAGGTGAA GATCCTTTTT GATAATCTCA TGACCAAAAT AAATTTTCCT AGATCCACTT CTAGGAAAAA CTATTAGAGT ACTGGTTTTA
fi cac8I sfaNI bl		fnu4HI haeIII/ nI bsoFI sau96I bbvI nlaIV bsrDI bsrI asuI CATTGCAGCA CTGGGGCCAG	nlaIV hgiCI banl mnli AGGTG CCTCAC	sau3Al  phi mbol/ndell  [[dam-] dpn[[dam+]  n-] dpni[[dam-]  ii alwi[dam-]  bstXl/xholi  mboli[dam-]  GTGAA GATCCTTTTT  CACTT CTAGGAAAA
msli maeiii AGCGT GACACC	foki acii bsri mnli GACTGGATGG AGGCGGATAA CTGACCTACC TCCGCCTATT	I II/mv I 236I GTAT CATA	ddel nlaIV mbol/ndeII[dam-] dpnI[dam+] hgiCI tru9I dpnII[dam-] banI mnlI mseI ACAGATGGCT GAGATAGGTG CCTCACTGAT TAA	rmal mael sau3Al mael sau3Al sau3Al hphl mbol/ndell[dam mbol/ndell[dam-] dpnl[dam+] dpnl[dam+] tru9l bstvl/xholl alwl[dam-] msel alwl[dam-] bstvl/xholl ahalll/dral bfal mboll[dam-] TTTAAAAGGA TCTAGGTGAA GATCCTTTTT GAT AAATTTTCCT AGATCCACTT CTAGGAAAAA CTA
6601 CGACG	fc bsr1 6701 GACTGC CTGACC	acil thal fnuDI bstUI bsh12 6801 CTCGCGG	se mk di di di 6901 ACAGA	tru9] mseI ahaII] 7001 TTTAA

```
mbol/ndell[dam-]
                                                                                                                              aluI
                                                                  dpnII[dam-]
                                                  dpnI[dam+]
                                                                                       alwI[dam-]
                                                                                                                                              TCAAAGGATC TICTIGAGAT CCTITITIC TGCGCGTAAT CTGCTGCTTG CAAACAAAAA AACCACGGCT ACCAGGGGTG GTTTGTTTGC CGGATCAAAA
AGTTTCCTAG AAGAACTCTA GGAAAAAAAA ACGCGCATTA GACGACGAAC GTTTGTTTT TTGGTGGCGA TGGTC3CCAC CAAACAAAG GCCTAGTTCT
                                                                                                                                                                                                                                                                                        CGATGGTTGA GAAAAAGGCT TCCATTGACC GAAGTCGTCT CGCGTCTATG GTTTATGACA GGAAGATCAC ATCGGCATCA ATCCGGTGGT GAAGTTCTTG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         7301 TCTGTAGCAC CGCCTACATA CCTCGCTCTG CTAATCCTGT TACCAGTGGC TGCTGCCAGT GGCGATAAGT CGTGTCTTAC CGGGTTGGAC TCAAGACGAT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AGACATOGTG GOGGATGTAT GGAGCGAGAC GATTAGGACA ATGGTCACOG ACGACGGTCA CCGCTATTCA GCACAGAATG GCCCAACCTG AGTTCTGCTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          7401 AGTIACCEGA TAAGGCGCAG CGGTCGGGCT GAACGGGGGG TTCGTGCACA CAGCCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             TCAATGGCCT ATTCCGCGTC GCCAGCCCGA CTTGCCCCCC AAGCACGTGT GTCGGGTCGA ACCTCGCTTG CTGGATGTGG CTTGACTCTA TGGATGTCGC
                                                                                                                                                                                                                                                                      7201 GCTACCAACT CTTTTCCGA AGGTAACTGG CTTCAGCAGA GCGCAGATAC CAAATACTGT CCTTCTAGTG TAGCCGTAGT TAGGCCACCA CTTCAAGAAC
          sau3AI
                                                                                                                              hpaII
                                                                                                                                                                                                                                   haeIII/palI
                                                                                                                                                                                                                                                                                                                                                                                                                                                          hinfI
                                                                                                                                                                                                                                                                                                                                                                                                                                       pleI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ddeI
                                                                                                                                                                                                                                                      haeI
                                                                                                                                                                                                                                                                                                                                                                                                               hpali
                                                                                                                                                                                                                                                                                                                                                                                                                                                        caull
                                                                                                                                                                                                                                                                                                                                                        SCLFI
                                                                                                                                                                                                                                                                                                                                                                                             Idsm
                                                                                                                                                                                                                                                                                                                                                                                                                                       dsaV
                                                                                                                                                                                                                                                                                                                                                                             ncil
                                                                                                             acil
                                                                                                                               nspBII
                                                                                                                                                                                                                                                      bslI
                                                                                                                                 acil
                                                                                                                                                                                                                                   maeI
                                                                                                                                                                                                                                                      bfaI
                                                                                                                                                                                                                 rmaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        aluI
                                                                                                                                                                                                                                                                                                                                                                                                                                                             bsrI
                                                                                                                                                                                                                                                                                                                                     fnu4HI
                                                                                                                                                                                                                                                                                                                                                           DSOFI
                                                                                                                                                                                                                                                                                                                                                                              bbvI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        alw441/snol
                                                                                                                                                                                                                                                                                                                                                                                                   fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                     alwNI[dcm-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        hgiAI/aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   apaLI/snoI
                                                                                                                                                                                                                                                                                                                                                                                                                                         bsrI bsoFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                             bbvI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           bsp1286
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              bsiHKAI
                                                                        cacel
                                                                                                                                                                                                                                                         hhal/cfol
                                                                                             fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   bmyI
                                                                                                                bsoFI
                                                                                                                                    bbvI
                                                                                                                                                                                                                                      hinPI
                                                                                                                                                                                                                                                                                                                                                                                                                                                           maelll
                                                      fnuDII/mvnI
                                                                                                                                  hhal/cfol
                                                                                            bsh1236I
                                                                           bstul
                                                                                                             hinPI
                                                                                                                                                                                                                                                       eco57I
                                mbol/ndell[dam-] thal
                                                                                                                                                     7101 TCAAAGGATC TTCTTGAGAT CCTTTTTTTC
                                                                                                                                                                                                                                         bsrI
                                                                                                                                                                                                                                                         maeIII
                                                                        dpnI[dam+] dpnI[dam+]
dpnII[dam-] dpnII[dam-]
                                                                                                                alwI[dam-]
                                                                                                                                    alwi[dam-] bstYi/xhoII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        hinPI bsiEI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                mnlI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      bbvI mcrI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    acil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         nspBII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           hhal/cfol
sau3AI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                bsoFI
                                                        mbol/ndell[dam-]
                   mboll[dam-]
                                                                                                                   bstYI/xhoII
                                                                                                                                                                                                                                                                                                                                                                                                                                                             acil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      hpall
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         bsaWI
```

# FIG. 48W

I [ [dcm+]			
scrFI mvaI ecoRII dsaV bstNI bsaJI aluI apyI[dcm+] gGAGCTTCCA	IV RGCCTATGGA TCGGATACCT	TGGATAACCG	oI AATACGCAAA TTATGCGTTT
bssSI hinPI mnlI hhal/cfoI AGCGCACGAG	nlaIV acii GATGCTCGTC AGGGGGGCGG AGCCTATGGA CTACGAGCAG TCCCCCCGCC TCGGATACCT		sapl hinPI mboll hhal/cfoI earl/ksp6321 mnli acii haeli GAGGAAGCGG AAGAGCGCCC AA
		TGCGTTATCC	mpli aci GAGGAAGCG
mspl hpall fnu4Hl bsll bsoFl bsaWl acil ATCCGTAAG CGCAGGGTC GGAACAGGAG	taqi mnli drdi hgal GTCGGGTTTC GCCACCTCTG ACTTGAGCGT CGATTTTTGT CAGCCCAAAG CGGTGGAGAC TGAACTCGCA GCTAAAAACA	haeIII/pall haeIII/pall fnu4HI scrFI bsoFI mval bsll acii dsav nlaIII fuuDII/mvnI bstNI haeIII/pall nspI bstUl bsh1361 nlaIV haeI cac81 aflIII cAACGCGCC TTTTTACGT TCCTGGCCTT TTGCTGCCACA TGTTCTTTCC GTTGCCCGA AAAATGCCA AGGACCGGAA AAACGAGGTGT ACAAGAAAGG	fnu4HI bsoFI bbvI pleI hinPI hinfI hhaI/cfoI AGCGCAGCGA GTCAGTGAGC
mspl hpall fi bsll be bsawl ac ATCCGGTAAG	ta rdi hgal ACTTGAGCGT TGAACTCGCA	nlaIII haeIII/pali nspI aeI nspHI 81 aflIII GGCCT TTTGCTCACA TG	
acii GCGGACAGGT CGCCTGTCCA	mnll drdI GCCACCTCTG AC	/pall haell cac8l TTGCTGGCCT	I mcrI bsiEI CGAACGACCG
	GTCGGGTTTC	haeIII/palI scrFI mval bslI ecoRII dsaV bstNI apyI[dcm+] nlaIV haeI GGT TCCTGGCCTT TTGC	fnu4HI bsoFI bbvI cac8I aciI rBI fnu4HI iI bsoFI GC TCGCCGAGC
hinPI hhal/cfoI haeII TGAGCATTGA GAAAGCGCCA CGCTTCCCGA AGGGAGAAAG	scrFI mvaI ecoRII dsaV bstNI apyI[dcm+] CCTGGTATCT TTATAGTCCT GGACCATAGA AATATCAGGA	haeIII/palI u4HI oFI i1 I bsll DII/mvnI UI 1236I GGCC TTTTTACGGT	cac! bsrBI acil acil TATTACCGCC TTTGAGTGAG CTGATACCGC
hinPI hhaI/c haeII GAAAGGGCCA			al TTTGAGTGAG
7501 TGAGCATTGA ACTCGTAACT	7601 GGGGGAAACG	cac8I 7701 AAAACGCCAG TTTTGCGGTC	fnu4HI bsoFI bsoFI bbvI cac8I aciI aciI aluI aciI bsoFI bsiEI 7801 TATTACCGCC TTTGAGTGAG CTGATACCGC TCGCCGCAGG CGAACGACCG ATAATGGCGG AAACTCACTC GACTATGGCG AGCGGCGTCG GCTTGCTGGC
7501	7601	7701	7801

# FIG. 48X

```
hhal/cfol asel/asnl/vspl
                                                                                                                                                                                 7901 CCGCCTCTCC CCGCGCGTTG GCCGATTCAT TAATCCAGCT GGCACGACAG GTTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT GGCGGAGAAGC GGCGCGCAAC CGCGAAAGGCG GCGCGCAAC TTACACTCAA TTACACTCAA TTACACTCAA
                                                                                                                                                    cac81
                                                                                                                                                                    acil
                                                                                                                                                                       bsrI
                                                                                                     cac8I
                                                                                                                                                  eael tfil asel/asnl/vspl
                                                                                                                                                                       cfrI hinfI mseI nspBII
                                                                                                                     aluI
                                                                                                                                      tru9I pvuII
                                                                                                                  bstUI haeIII/pall
fnuDII/mvnI
                                                                                                  fnuDII/mvnI
                                                                    hhal/cfol
                                  bsh12361
                                                                                                                                     bsh1236I
                  bstui
                                                    hinPI
                                                                                                                                                         bslI
aciI
                                                                                       thaI
                                                                                                                                                        mnlI
```

FIG. 48Y

8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA TGGAGTGAG AACCGTGGG GTCCGAAATG TGAAATACGA AGGCCGAGCA TACAACACC CTTAACACTC GCCTATTGTT AAAGTGTGTC CTTTGTCGAT

mspI hpaII

hgiCI apyI[dcm+]

banl bsaJI

dsav nlaIV bstNI

ecoRII

SCLFI

mvaI

aciI bsrBI

```
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727 4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248 5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804 7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340 3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590 5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
                                                                                                                                                                                                                                                                                                                                                 823 1039 2738 4237
217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       988 1690 1858 5117 5947 6329
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ahalii/drai(TTTAAA): 696 4935 6290 6982 7001
ahdi/eam11051(GACNNNNGTC): 2087 6865
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1876 5651 6198 7444
                                                                                                                                                                                                                                                                                                                         2969 3967 4529
                                                           aseI/asnI/vspI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     see hinli
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         932 7758
tru9I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          1833
                            mseI
                                                                                                                                            8101 TGACCATGAT TACGAATTAA
                                                                                                           asp700
                                                                                                                                                                          ACTGGTACTA ATGCTTAATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 984
                                                                                         XmnI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         ahaII/bsaHI (GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    alw441/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 aflii/bfri(CTTAAG):
                                                                                                                    nlaIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              aflii(ACRYGT):
                                                                                                                                                                                                                                                                                                                           acc651 (GGTACC):
                                                                                                                                                                                                                                                                                            aatII(GACGTC):
                                                                                                                                                                                                                                   >length: 8120
                                                                                                                                                                                                                                                                                                                                                          accI(GTMKAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                    acil(CCGC):
```

FIG. 48Z

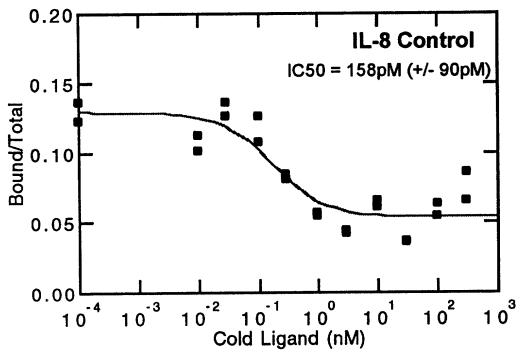


FIG. 49A

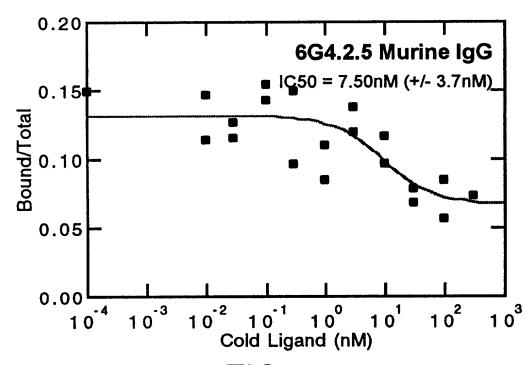


FIG. 49B

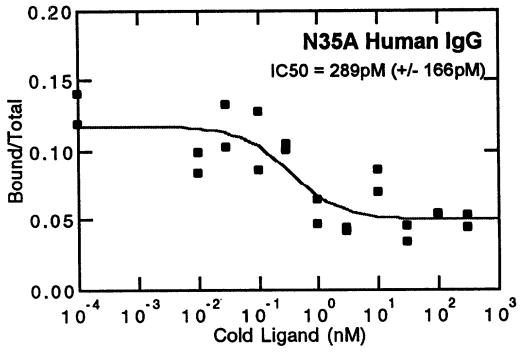


FIG. 49C

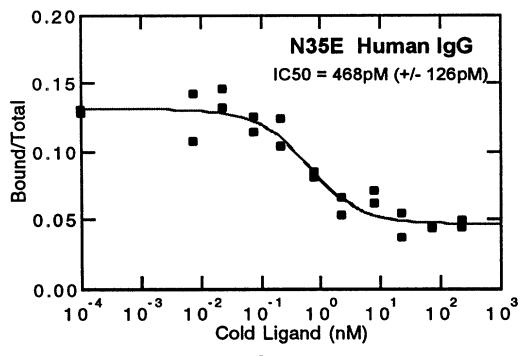
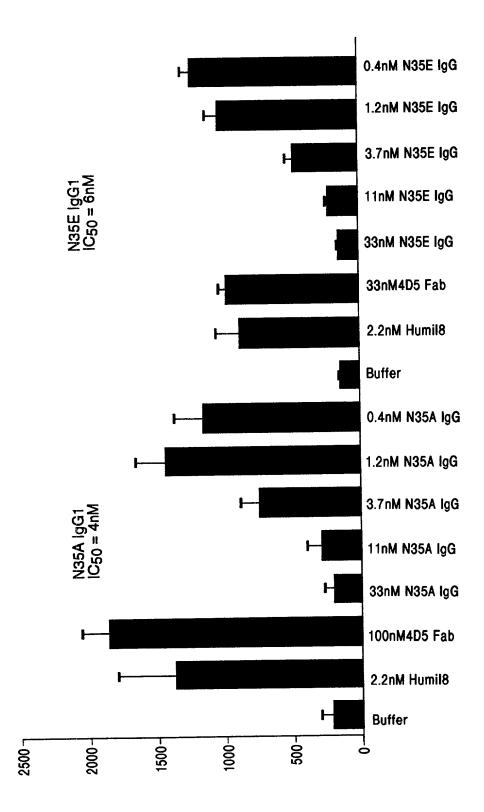
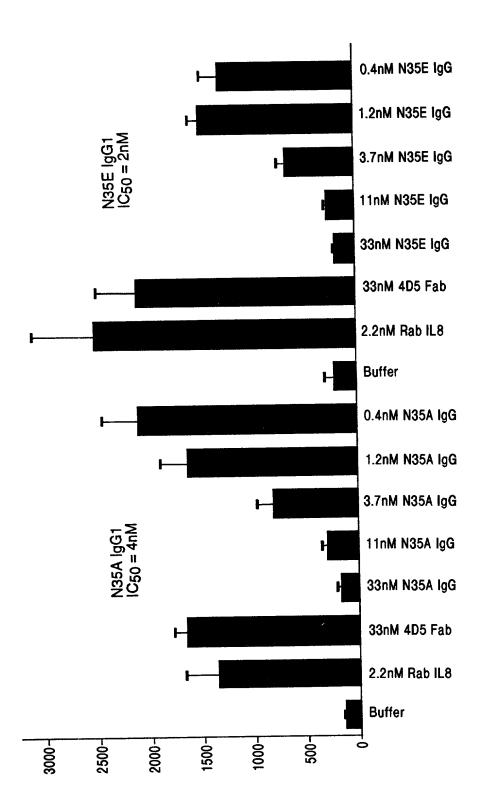


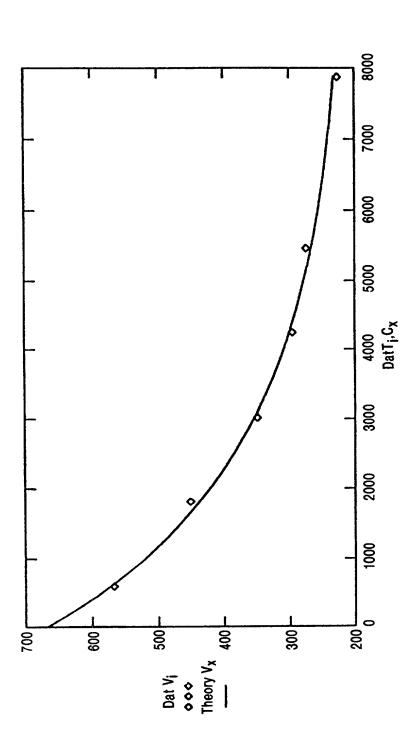
FIG. 49D



### FIG. 50A

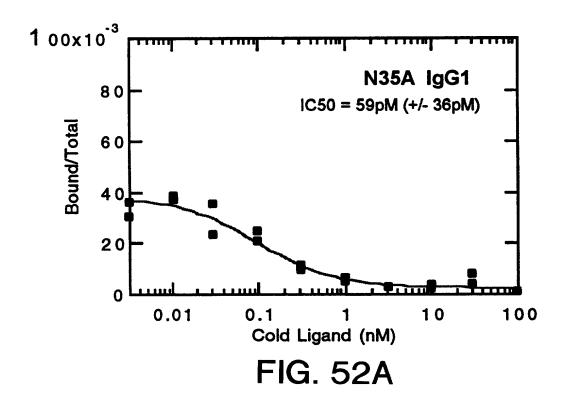


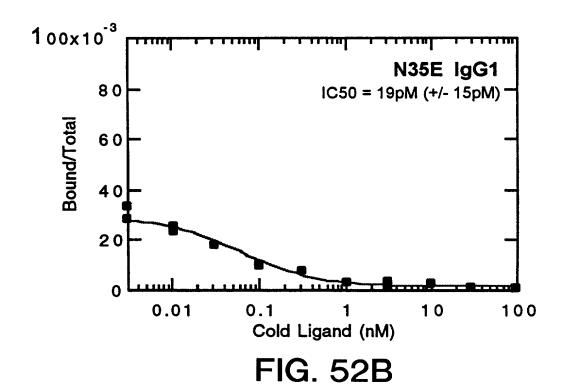


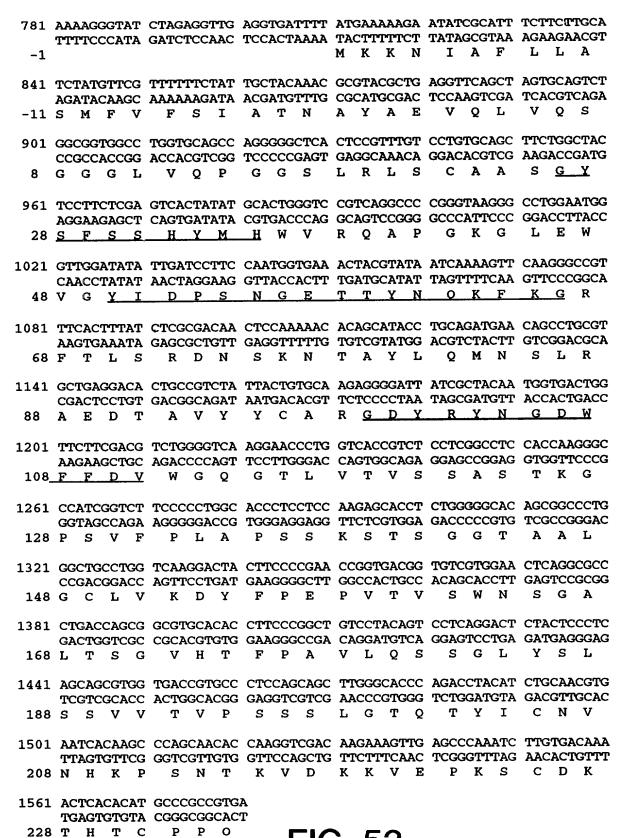


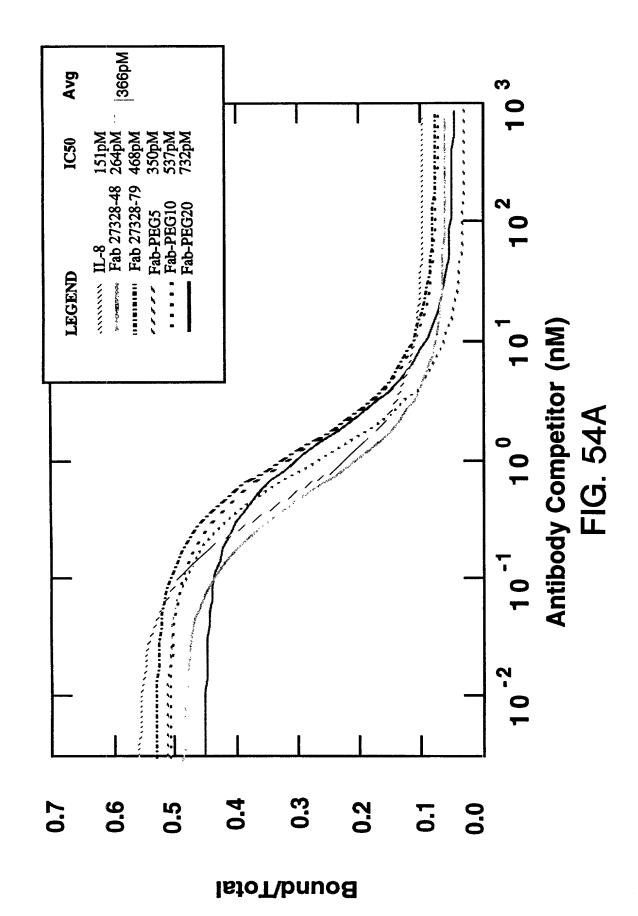
Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

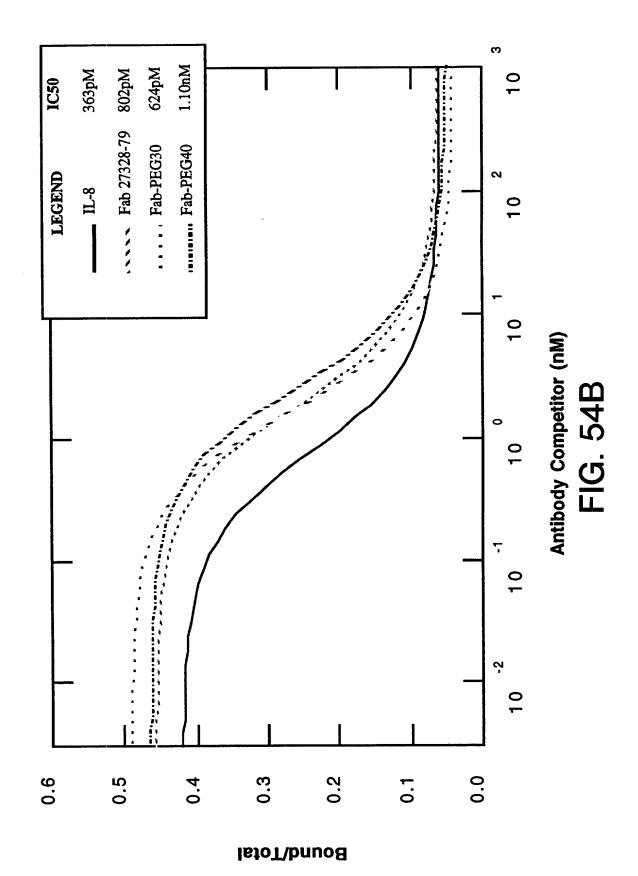
		FIG. 5	
Kd	350pM	88pM	49pM
kď	2.9x10-4	$7.7x10^{-5}$	$1.4x10^{-4}$
ka	8.3x10 <sup>5</sup>	$8.7x10^{5}$	$3.0 \times 10^6$
SAMPLE	Murine 6G4.2.5 IgG2a	6G4V11N35A-IgG1	6G4V11N35E-IgG1

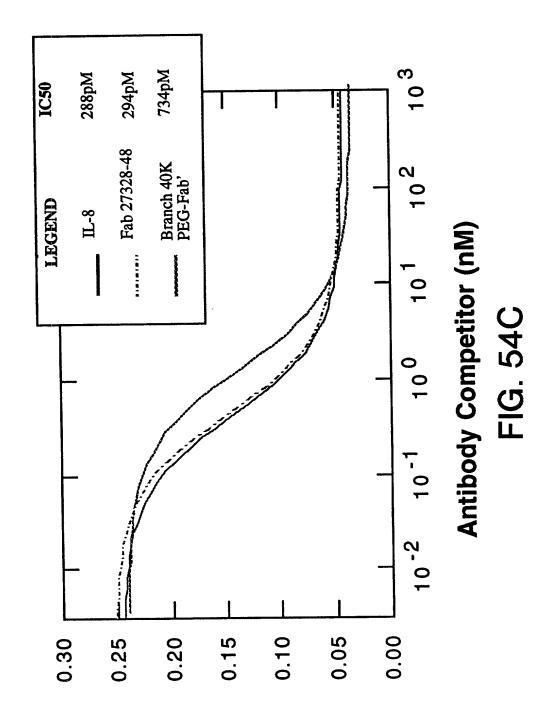




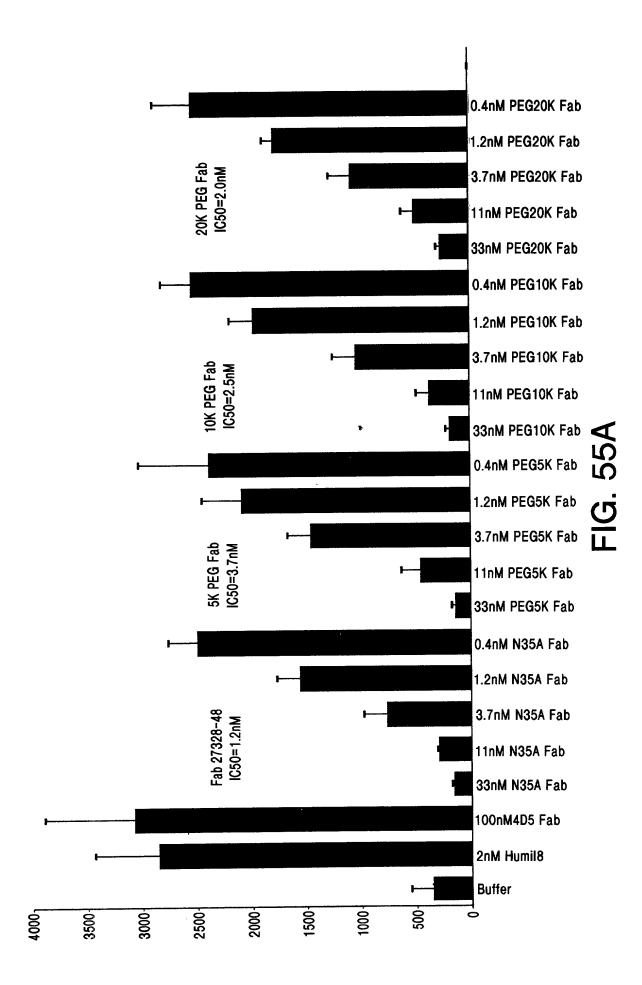


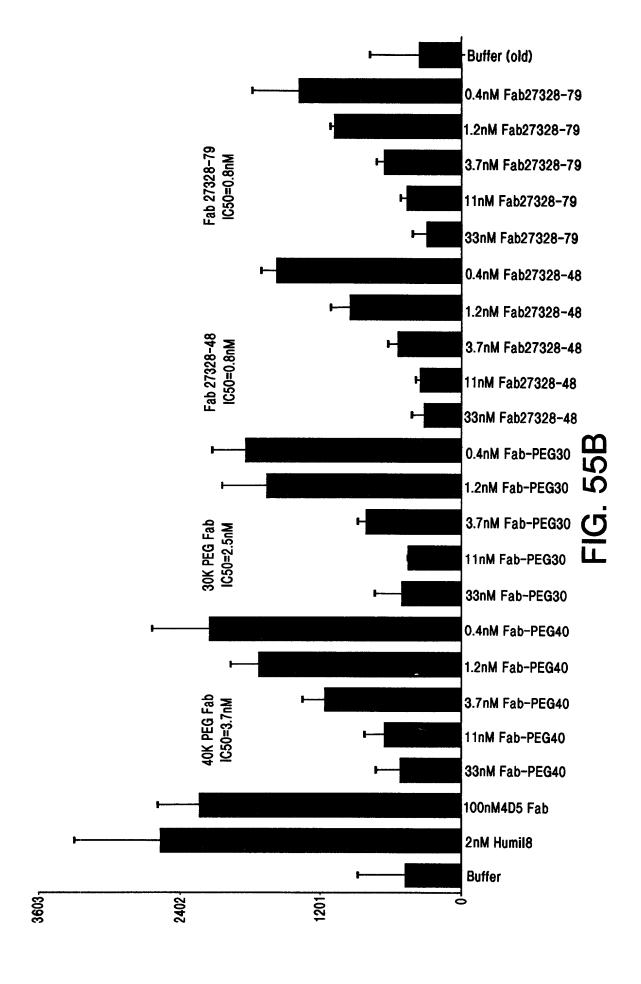


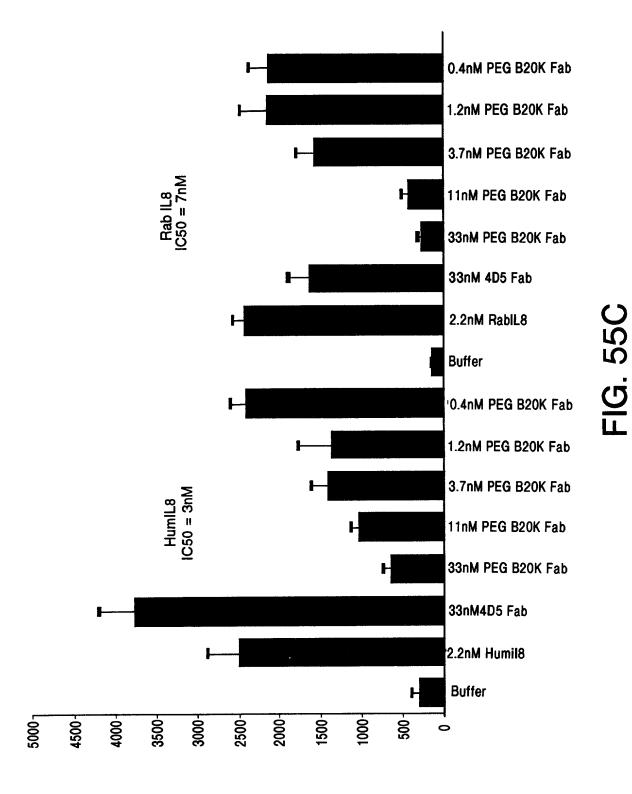


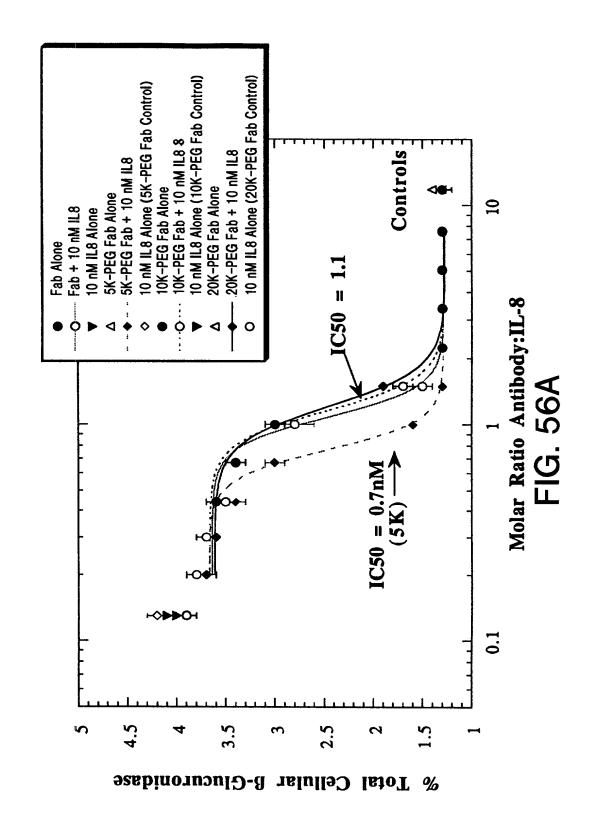


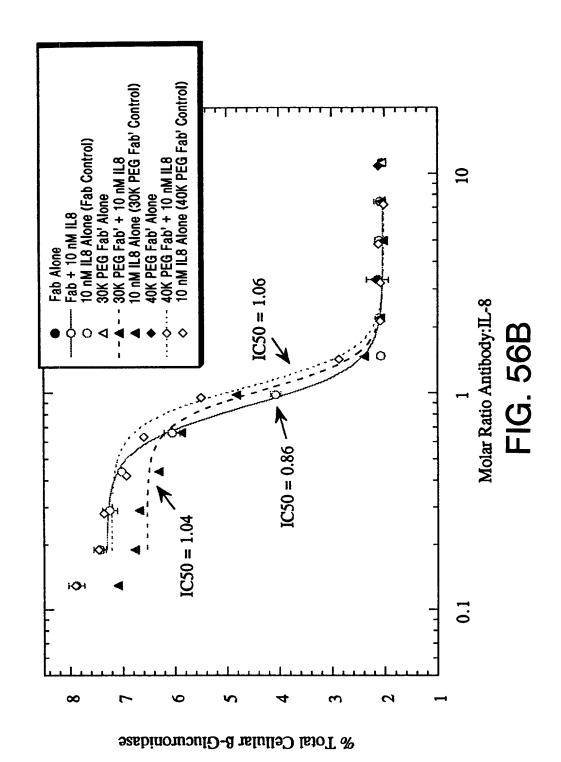
**Bound/Total** 









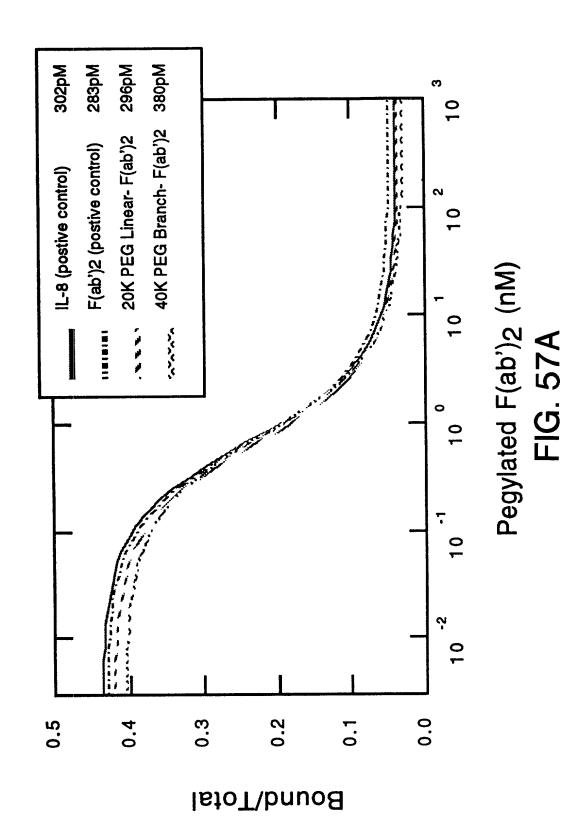


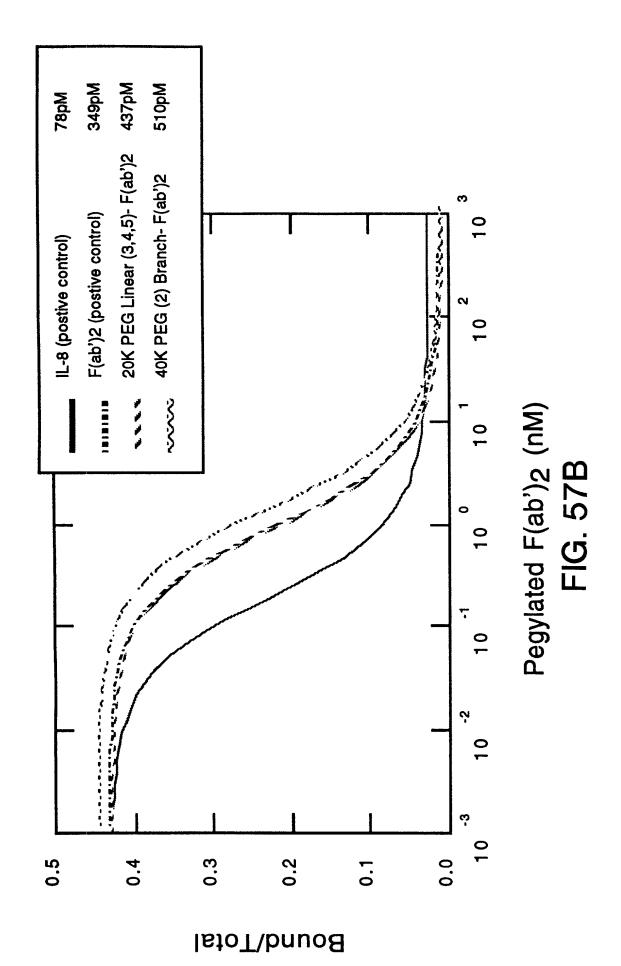
IL8 Alone (Fab Control)

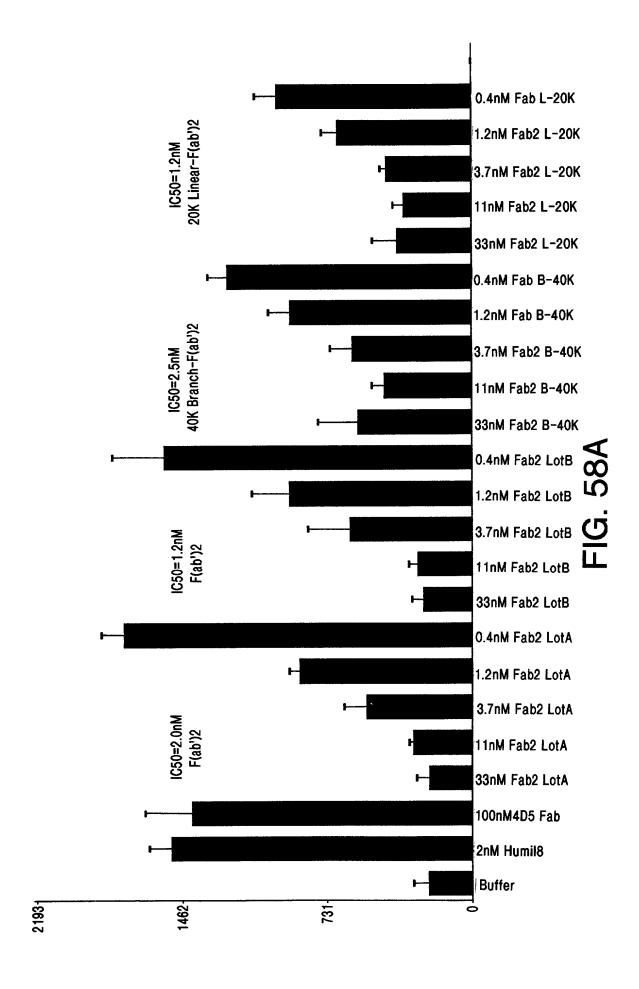
— Fab + 10 nM IL8

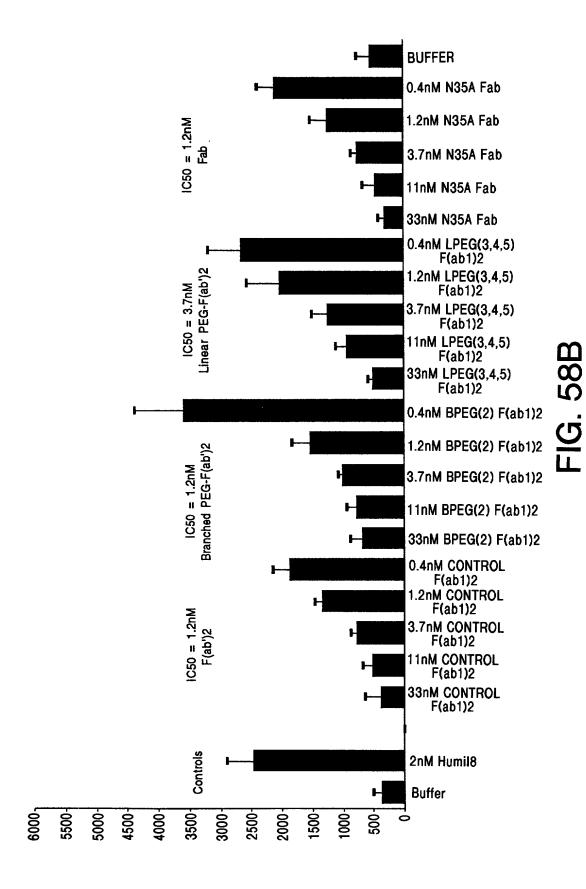
Fab Alone
IL8 Alone (40K Br PEG Fab' Control) 40K Branched PEG Fab' IC50 = 1.144 40K Br PEG Fab' + 10 nM IL8 10 40K Br PEG Fab' Alone Molar Ratio Antibody:IL8 FIG. 56C Fab Control IC50 = 0.832 0.1 00

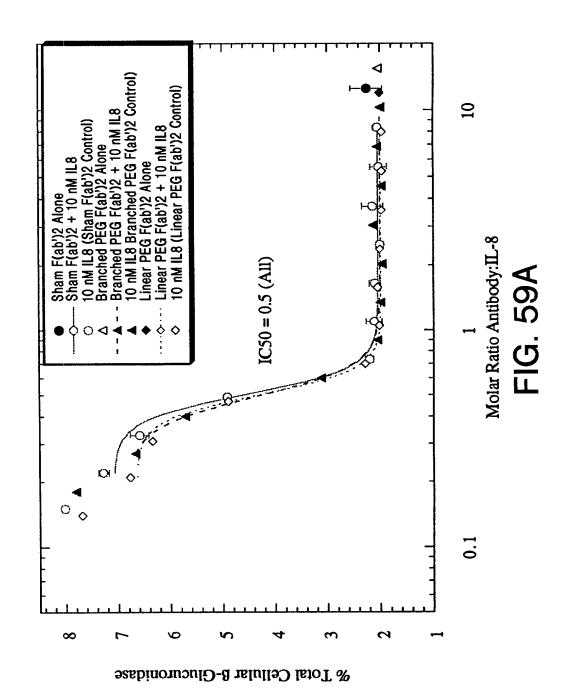
% Total Cellular b-Glucuronidase Activity

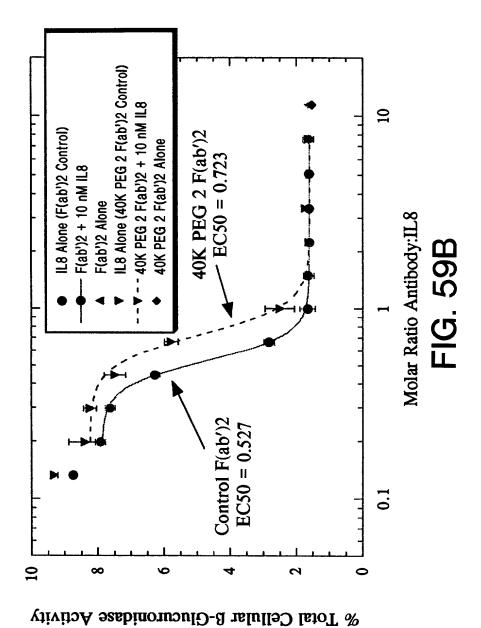


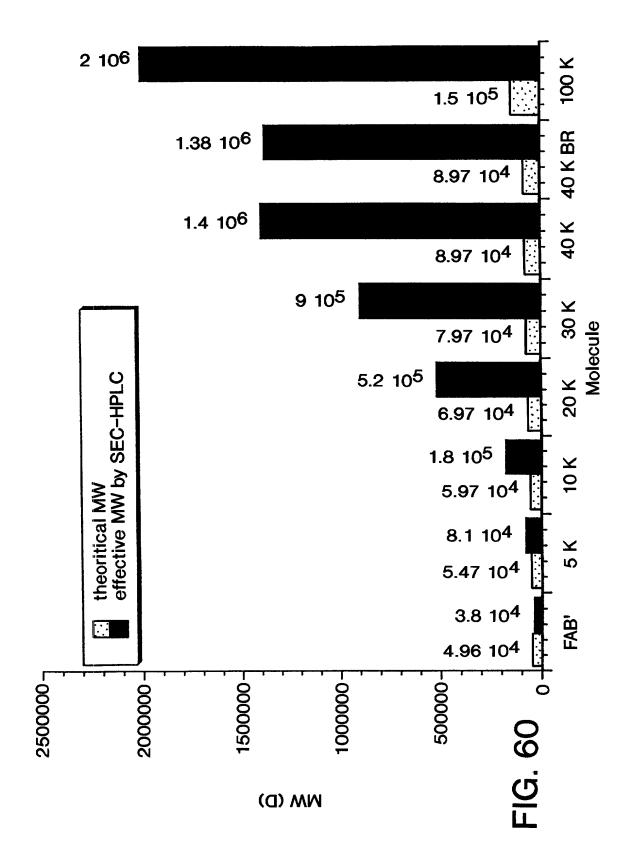


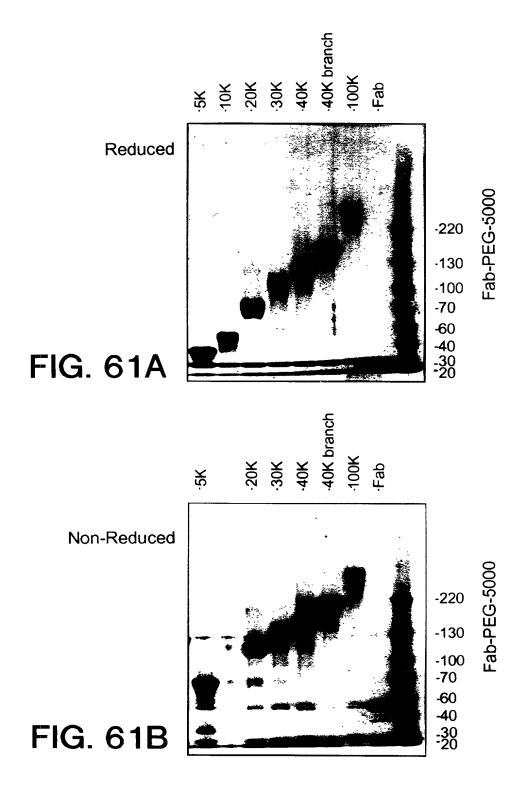


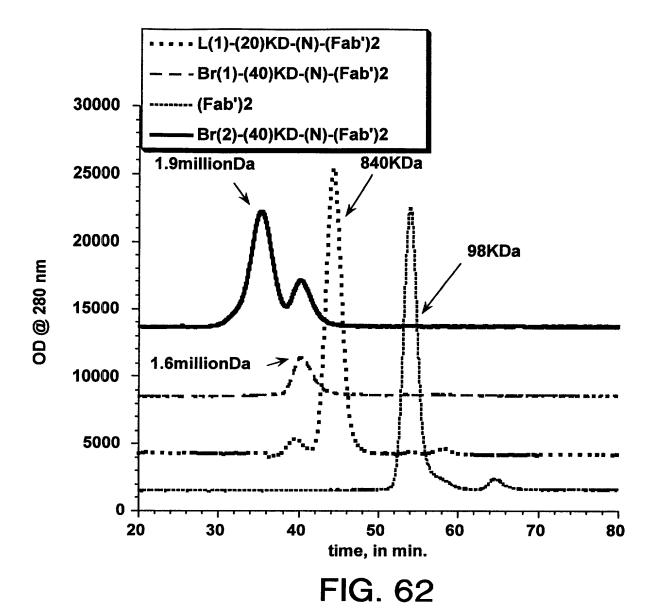












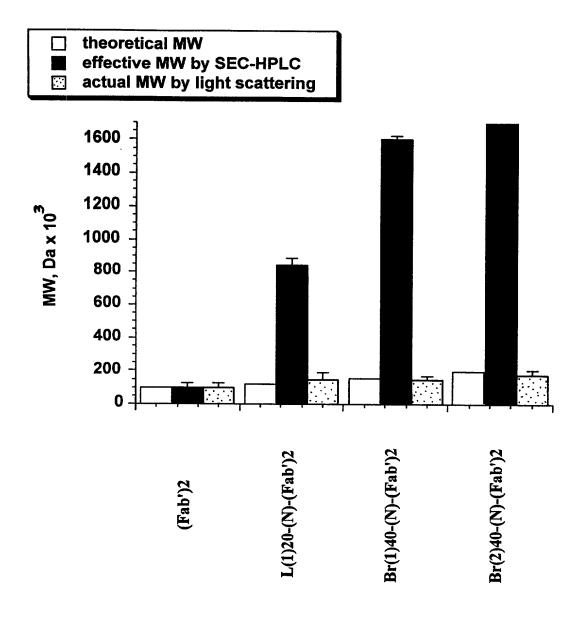


FIG. 63

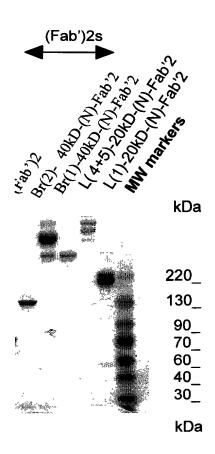
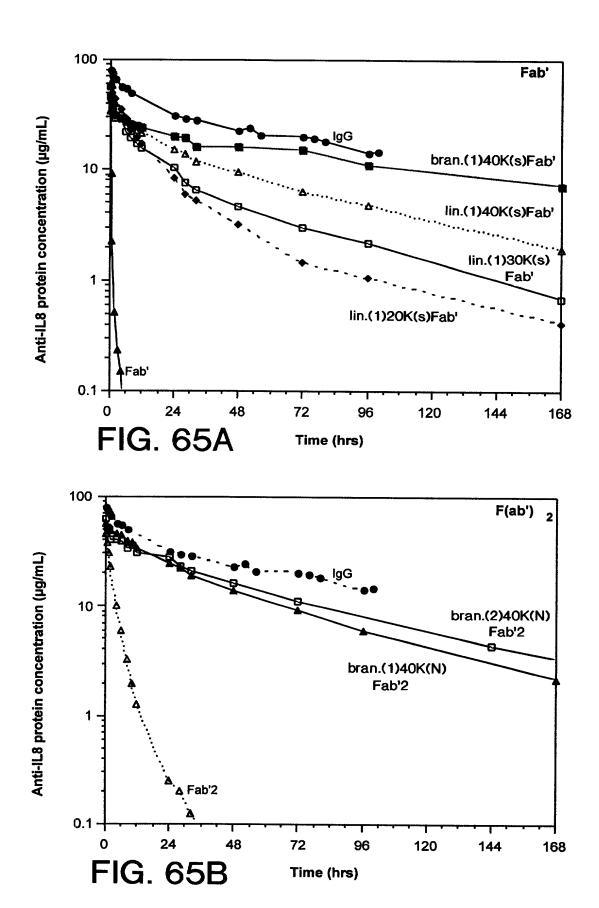


FIG. 64



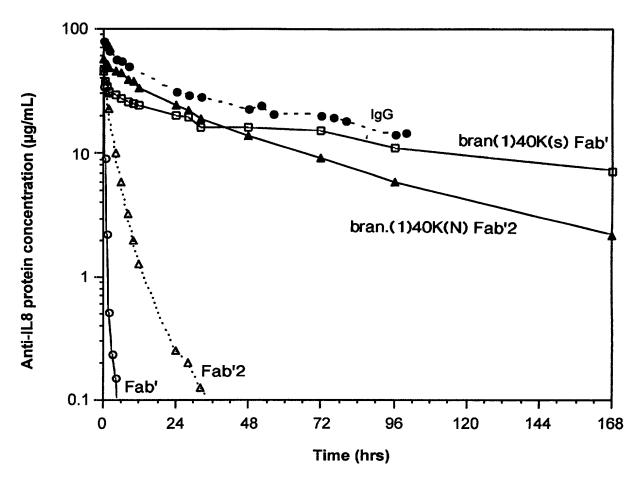
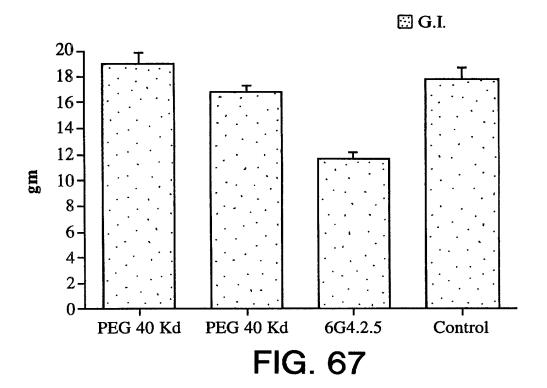
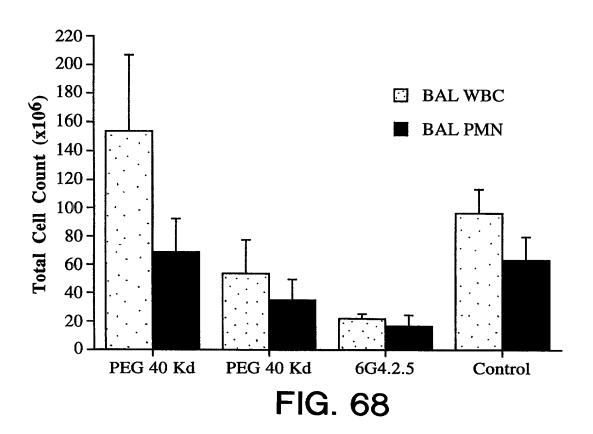


FIG. 66





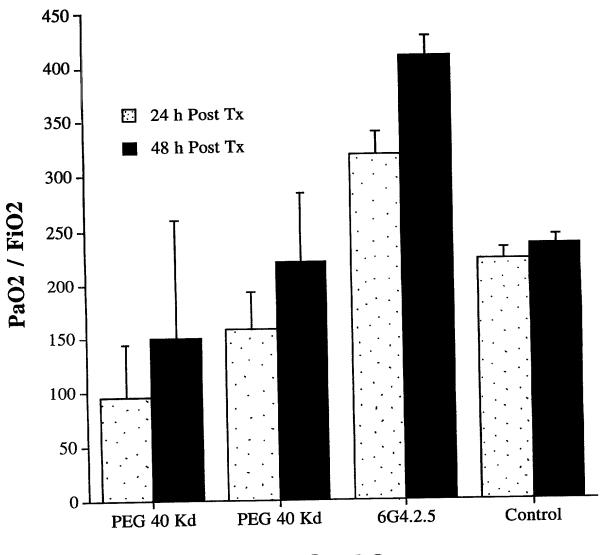
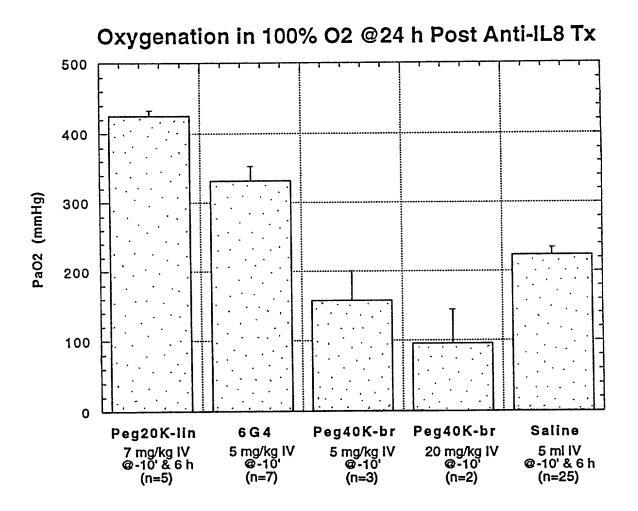


FIG. 69



**FIG. 70A** 

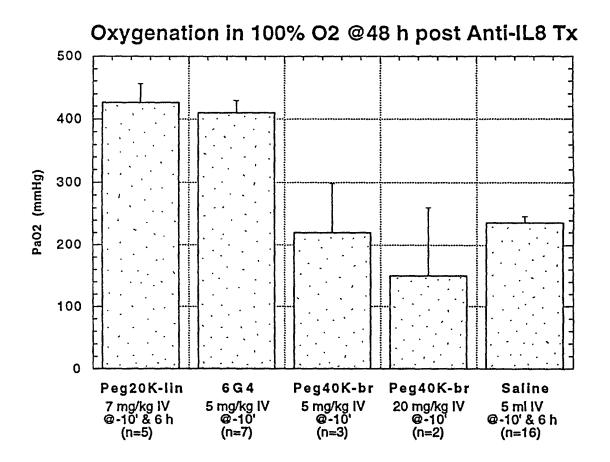


FIG. 70B

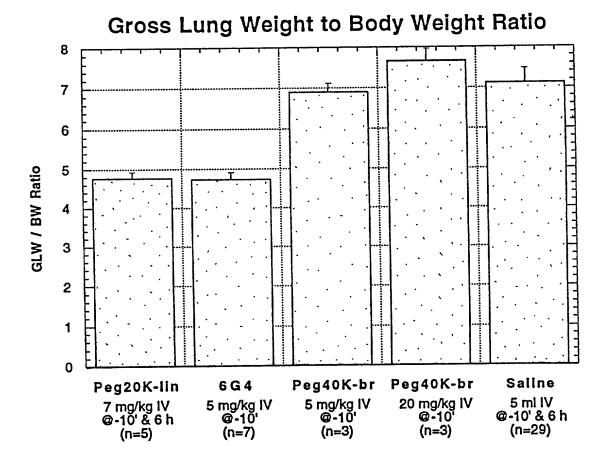


FIG. 70C

## Total WBC in BAL Fluid 200 150 Total Cell Count (10e6) 100 50 0 Peg20K-lin Peg40K-br Peg40K-br 6 G 4 Saline 5 mg/kg IV @-10' (n=3) 20 mg/kg IV @-10' (n=3) 7 mg/kg IV @-10' & 6 h (n=5) 5 mg/kg IV @-10' (n=7) 5 ml IV @-10' & 6 h (n=11)

FIG. 70D

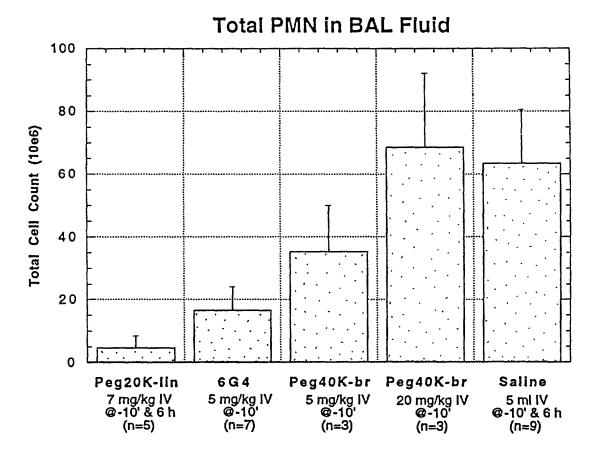
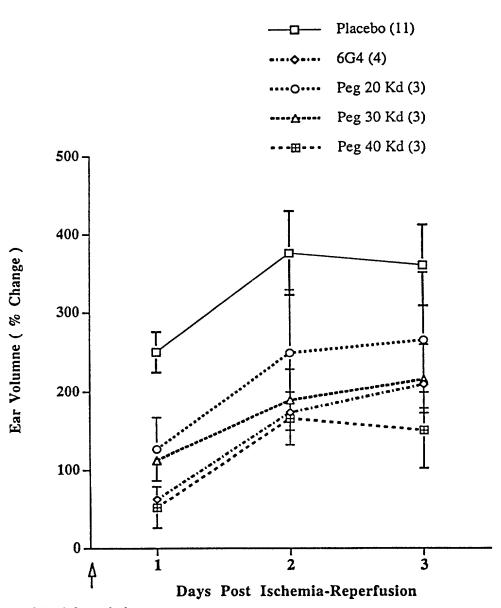


FIG. 70E

## The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations: Single Dose (5 mg/kg) administered IV at time of reperfusion

FIG. 71